

## Transcript of October 17, 2000 Meeting

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ELECTRICAL STIMULATION FOR THE TREATMENT OF WOUNDS

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HEALTH CARE FINANCING ADMINISTRATION

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Medicare Coverage Advisory Committee

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Medical and Surgical Procedures Panel

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October 17, 2000

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Baltimore Convention Center

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Baltimore, Maryland

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Panelists

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Chairperson

Alan M. Garber, MD, PhD

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Vice-Chairperson

4

Michael D. Maves, MD, MBA

5

Voting Members

6

Angus M. McBryde, MD, FACS

H. Logan Holtgrewe, MD, FACS

Kenneth P. Brin, MD, PhD

Les J. Zendle, MD

Bruce Sigsbee, MD

Consumer Representative

Phyllis E. Greenberger, MSW

Industry Representative

Marshall S. Stanton, M.D.

Non-Voting Guest

Adrian Oleck, MD

Director, Coverage and Analysis Group, HCFA

Sean R. Tunis, MD, MSc

Executive Secretary

Constance A. Conrad, RN

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1                   P R O C E E D I N G S

2                   MS. CONRAD: Good morning. Welcome to the

3 panel chairperson, members and guests. I am

4 Constance Conrad, Executive Secretary of the Medical

5 and Surgical Procedures Panel of the Medicare

6 Coverage Advisory Committee. The panel is here today

7 to provide advice and recommendations to the Health

8 Care Financing Administration regarding electrical

9 stimulation regarding electric stimulation for the

10 treatment of wounds.

11                   At the conclusion of today's session,

12 panel members will be asked to vote on a series of

13 questions. The answers to those questions will

14 constitute this panel's recommendation which will be

15 submitted to the Executive Committee when it meets.

16 When the Executive Committee ratifies the  
17 recommendation, it will officially transmit that  
18 recommendation to HCFA. HCFA will develop a coverage  
19 policy within 60 days of the receipt of that  
20 recommendation.

21 For the purposes of today's panel,  
22 Dr. Adrian Oleck, medical director of the durable  
23 medical equipment regional carrier for Region B and  
24 noted expert in the field of wound healing received  
25 an appointment of temporary nonvoting member status.

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1 Dr. Oleck's expertise will enhance this panel's  
2 deliberative process.

3 The following announcement addresses  
4 conflict of interest issues associated with this  
5 meeting, and is made part of the record to preclude  
6 even the appearance of impropriety. To determine if  
7 any conflict existed, the Agency reviewed the  
8 submitted agenda and all financial interests reported  
9 by the panel participants. The conflict of interest  
10 statutes prohibit special government employees from  
11 participating in matters that could affect their or  
12 their employer's financial interests. The Agency has  
13 determined that all members and consultants may  
14 participate in the matters before this panel today.

15 With respect to all other participants, we  
16 ask in the interest of fairness that all persons  
17 making statements or presentations disclose any  
18 current or previous financial involvement with any  
19 firm whose products or services they may wish to  
20 comment on.

21 Now, a few words from Sean Tunis, the  
22 Director of the Coverage and Analysis Group.

23 DR. TUNIS: Good morning. I guess today  
24 we have here the subset of people who could actually  
25 find this room, so congratulations for making your

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1 way here.

2 I just wanted to make a couple of comments  
3 before Dr. Garber spoke related to the recently  
4 issued Medicare coverage decision memorandum on the  
5 two technologies for -- the two previous technologies  
6 for urinary incontinence, pelvic floor electrical

7 stimulation and biofeedback. And there has been,  
8 just to sort of clarify, you know, in public, sort of  
9 what was laid out in the text of the decision memo in  
10 terms of the rationale for those coverage decisions.

11 As many of know, at a meeting of this  
12 Medical Surgical Panel where those two technologies  
13 were discussed, the conclusion of the panel was that  
14 the scientific evidence for the effectiveness for  
15 both pelvic floor electrical stimulation and  
16 biofeedback was inadequate to make a conclusions  
17 based solely on the scientific evidence. The way  
18 that those questions were framed to the panel and the  
19 way that we discussed them internally, and the way  
20 the trials were designed, really addressed the  
21 question of these technologies for primary therapy of  
22 patients with urinary incontinence, in other words,  
23 looking at this as an initial intervention.

24 There really was no studies, or maybe a  
25 single study that had any evidence at all about the

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1 effectiveness of those therapies for patients who had  
2 failed pelvic muscle exercises or conservative  
3 therapy, and so the coverage decision essentially was  
4 that for initial therapy, or for primary therapy of  
5 urinary incontinence, pelvic floor electrical  
6 stimulation remained noncovered, and biofeedback  
7 remained at carrier discretion, unchanged from  
8 previous coverage policy.

9 However, for patients who had failed  
10 conservative therapy with pelvic muscle exercises, or  
11 were unable to perform them, the decision was to  
12 provide Medicare coverage in those circumstances.

13 And just to lay out clearly what the  
14 rationale was for positive coverage under that set of  
15 conditions, the considerations that went into that  
16 were four major considerations. One was that there  
17 were in fact some positive supportive studies for  
18 both technologies. There were also obviously  
19 negative studies, studies that showed no benefit.  
20 However, there were at least one or two randomized  
21 control, placebo control studies that showed some  
22 benefit, particularly for pelvic floor electrical  
23 stimulation.

24 We took that then in the context of a  
25 second consideration, which is patients that failed  
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1 pelvic muscle exercise have very few other  
2 nonsurgical options, and so these technologies  
3 represented a possibility at least of a relatively  
4 harmless nonsurgical alternative for an important  
5 problem, and we took that into account as well.

6 The third consideration we already  
7 mentioned, was essentially there really was no  
8 suggestion that either biofeedback or pelvic floor  
9 electrical stimulation had a significant risk of  
10 harm, and finally, that there was very consistent and  
11 very strong expert testimony and consensus from  
12 professional organizations that supported both  
13 feedback and pelvic floor stimulation.

14 So those are kind of the four  
15 considerations that went into this narrowly defined  
16 positive coverage for patients who failed  
17 conservative therapy, and I just wanted to sort of  
18 lay that out clearly in public.

19 And then finally, we do say in the  
20 decision memo, and we are quite interested in  
21 following up on this, that we would in fact like to  
22 see the studies done that confirm the effectiveness  
23 of either of these technologies in patients who  
24 failed pelvic muscle exercise or in fact, better  
25 studies that clearly demonstrate the effectiveness of

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1 either one for primary therapy. So that's just as a  
2 wrap-up on those two coverage decisions.

3 And with that, I think Alan, Dr. Garber  
4 has some opening material as well.

5 DR. GARBBER: Thank you, Sean. I think I  
6 can be very brief. I thought it would be helpful  
7 just to give a little progress report about what is  
8 going on with the Executive Committee and I think  
9 some of you but perhaps not all of you know that the  
10 Executive Committee when they drafted the interim  
11 guidelines for how the panels should conduct their  
12 business, they also had emphasized that these  
13 guidelines could be changed, and in fact, our  
14 previous panel meeting was the first opportunity to

15 really test out the guidelines that the Executive  
16 Committee had developed.

17 And in the wake of that, I know you are  
18 all aware of the Executive Committee's decisions to  
19 ratify the conclusions of this panel, but there was  
20 considerable discussion both at the last panel  
21 meeting and at the Executive Committee meeting. A  
22 subcommittee was formed from the Executive Committee  
23 to take a look at the interim guidelines and see how  
24 if at all they should be changed. That subcommittee  
25 has not issued its reports yet, and it should be

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1 ready in time for the Executive Committee meeting in  
2 November. And after that meeting, we will have a  
3 better idea of where the Executive Committee stands  
4 on changing these guidelines.

5 If it wouldn't be out of order, I'd like  
6 to just mention a few of the things that are under  
7 consideration. Would that be appropriate?

8 For the most part -- well, actually the  
9 direction in which I think the subcommittee is going  
10 is pretty much to preserve the essential features of  
11 the existing interim guidelines, in particular the  
12 emphasis on the two major questions about adequacy of  
13 evidence and also if the evidence is adequate, what  
14 is the size of the health effect. There are many  
15 criticisms, comments, suggestions that have come to  
16 HCFA and to the Executive Committee, about these  
17 should be changed, about how the recommendations  
18 should be changed, and although the central part of  
19 it will not fundamentally be changed as I see it, in  
20 the current direction of the subcommittee, there will  
21 be much more discussion about types of evidence, and  
22 I think it will accommodate many of the concerns that  
23 people have expressed, that the types of evidence  
24 that would be considered are construed too narrowly,  
25 that only a very narrow range of evidence would be

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1 considered. And so, I think you will see a more  
2 explicit statement about additional kinds of evidence  
3 that should be considered in the panel deliberations.

4 There is one substantive change that I  
5 will mention, and it's partly because I'm the person

6 who actually pushed for this, but I think there is a  
7 consensus, and that is when the panel concludes that  
8 the evidence is not adequate, that there are  
9 circumstances in which they should give more  
10 information in order to give HCFA guidance.

11 For example, the evidence may be  
12 inadequate because, simply because studies have not  
13 been conducted that either have a large number of  
14 study subjects, they may have design flaws, there may  
15 be numerous reasons why the panel concluded they were  
16 not adequate to draw conclusions. Yet, it might be  
17 possible to conduct studies and there may be reasons  
18 for HCFA to decide to go ahead and cover the  
19 technology either within the context of the study,  
20 and there's of course precedent for that, that is,  
21 they would fund coverage only if the procedure or the  
22 intervention is performed in the context of say an  
23 NIH approved study, or they might determine to cover  
24 it and revisit the issue after adequate time had  
25 elapsed for good studies to be conducted that would

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1 enable panels to draw conclusions.

2 The Executive Committee I don't think is  
3 going to try to tell HCFA what they should do, but if  
4 HCFA should decide that they want to make a decision  
5 to cover in some form, even though the evidence is  
6 inadequate, we might be able to give them more  
7 helpful guidance that look, this particular  
8 procedure, although the evidence is inadequate, looks  
9 very promising. The idea is that this kind of  
10 designation might be used on a selective basis where  
11 for example, it's a very promising procedure, good or  
12 service, or it might be one with very little risk and  
13 again, substantial potential benefit, even though the  
14 studies are inadequate.

15 If any of you have further comment about  
16 how the Executive Committee interim guidelines should  
17 be changed, please send them in. Many of you have  
18 commented already; there is still ample time to make  
19 changes before this goes to the Executive Committee  
20 and certainly in the context of the Executive  
21 Committee meeting itself. In the meantime, I believe  
22 that the current guidelines of the Executive



23 Committee stand and the questions that you will hear  
24 about that were proposed to the panel today are  
25 basically a direct translation of the Executive

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1 Committee's questions set in the context of  
2 electrical stimulation for chronic wounds. Thank  
3 you.

4 MS. CONRAD: I now ask the panel members  
5 to introduce themselves, starting, let's start at the  
6 far end. Phyllis?

7 MS. GREENBERGER: Phyllis Greenberger,  
8 Executive Director for the Society for Women's Health  
9 Research.

10 DR. STANTON: Dr. Marshall Stanton,  
11 Medical Director for Medtronic, industry  
12 representative on this panel.

13 DR. OLECK: Dr. Adrian Oleck, medical  
14 director of the Medicare regional carrier, Region B.

15 DR. ZENDLE: Dr. Les Zendle, Associate  
16 Medical Director of Southern California Permanente  
17 Medical Group, in Los Angeles.

18 DR. BRIN: Dr. Kenneth Brin, a practicing  
19 cardiologist, Summit Medical Group, Summit, New  
20 Jersey.

21 DR. MCBRYDE: Dr. Angus McBryde,  
22 orthopedic surgeon at the University of South  
23 Carolina, Columbia.

24 DR. HOLTGREWE: Logan Holtgrewe, urologist  
25 on the faculty of Johns Hopkins, here in Baltimore.

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1 DR. MAVES: Mike Maves, vice chair, and  
2 president of the Consumer Healthcare Products  
3 Association.

4 DR. SIGSBEE: Bruce Sigsbee, practicing  
5 urologist, member of Salt Marsh Medical Associates in  
6 Hyannis, Massachusetts.

7 DR. GARBER: I guess I have already  
8 mentioned this. Alan Garber, chair, Department of  
9 Veterans Affairs and Stanford University.

10 MS. CONRAD: Sean and Connie.

11 Proceeding with the agenda, Rita Frantz.  
12 Dr. Frantz is going to offer an overview of  
13 electrostimulation for the treatment of wounds.

14 DR. FRANTZ: Good morning. It's my  
15 pleasure to be here this morning. And my task is  
16 simply give, as I was directed by Connie Conrad and  
17 others, to simply give you an overview of the role of  
18 electrical stimulation in chronic wound healing, and  
19 I promise to stay within the time limits of the  
20 agenda.

21 We'll get our technology squared away  
22 here. I think it would be safe to say as an opening  
23 remark that electrical stimulation is largely an  
24 unknown and a poorly understood treatment modality  
25 for the treatment of chronic wounds. Appreciation of

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1 its potential contribution to promotion of chronic  
2 wound healing has been limited in the scientific  
3 community as well as within the provider community  
4 due to a lack of familiarity with the specialized  
5 body of knowledge. So today I would like to just  
6 review with you briefly some of the points that one  
7 can take from a review of this literature.

8 First of all, I want to just describe a  
9 little bit about how electrical stimulation works,  
10 and you introducing yourselves this morning, it's  
11 obvious you all come from quite a variety of  
12 backgrounds and may not be familiar with this  
13 particular technology and how it's used in wound  
14 healing.

15 Secondly, I'd like to review for you  
16 briefly the treatment modalities, how they're applied  
17 to chronic wounds and then look at how effective  
18 electrical stimulation can be in promoting various  
19 types of chronic wounds and their progression towards  
20 healing.

21 How does electrical stimulation work?  
22 Well, there are innumerable laboratory and clinical  
23 studies that establish that electrical stimulation  
24 has a positive effect, both at the cellular level and  
25 in the whole overall repair process. Briefly, these

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1 studies show us that fibroblast activity is enhanced  
2 and actually stimulated by use of electrical current  
3 and that wound contraction is facilitated. Studies  
4 done at the University of Miami have established that

5 there's actually an increase in protein and DNA  
6 synthesis in a human fibroblast when it's stimulated  
7 with electrical current and that in fact, receptor  
8 sites on the fibroblast actually are increased for  
9 transforming growth factor beta, which is some  
10 exciting new work that was recently published.

11 Now the overall effect that this then has  
12 on the repair process is to improve the organization  
13 of collagen, that protein network that forms the new  
14 wound bed. It also increases the tensile strength or  
15 the strength of the scar as -- it also improves blood  
16 flow and reduces edema. Now when we look at the  
17 tissue level, which is where most of us spend our  
18 time, the effect of electrical stimulation is that it  
19 is believed to actually restart or accelerate the  
20 wound heal process by initiating and imitating the  
21 natural electrical current that occurs in the skin.

22 And researchers in the early 1980s  
23 actually established that on the skin surface, there  
24 is an endogenous built-in bioelectric system, and you  
25 see this illustrated here from the works of Fulton

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1 and Baker, who showed that on the skin surface, the  
2 skin carries more negatively charged, is more  
3 negatively charged than are the deeper skin layers,  
4 and in fact, the average voltage on the skin is  
5 approximately 23 millivolts. This occurs because of  
6 the positively charged sodium ions that are present  
7 in perspiration actually being pumped through some of  
8 the superficially layers of the epidermis, and the  
9 deeper cells then are left positive in relation to  
10 the chloride ions left on the skin surface which are  
11 negative, creating what is often referred to as the  
12 skin battery, again, because of the positive and  
13 negative poles on a battery.

14 Now the separation of the positively  
15 charged wound tissue from the negatively charged  
16 peri-wound skin around the skin, around the wound,  
17 creates a low level of bioelectric current. And this  
18 current when injury occurs, we have the positively  
19 charged ions in the injured dermis exposed, and the  
20 combination of the positively charged ions in the  
21 wound and the negative charge of the outer layer of

22 skin creates a skin battery that drives this  
23 electrical current as you see here. And this was  
24 described in Jaffe and Vanable's work in 1984.

25 The bioelectric current that we see  
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1 illustrated here, this natural skin battery, is  
2 actually facilitated by the presence of a moist wound  
3 environment and the use of an electrically conductive  
4 solution in a wound bed, such as normal saline, is  
5 thought to facilitate this bioelectric process, and  
6 actually promote the normal bioelectric system of the  
7 body.

8 Now, in vitro studies show us that cells  
9 in culture are actually attracted to the electrical  
10 charges of the body and that by applying electrical  
11 current, you actually can enhance the migration of  
12 cells into the wound bed, this what's called  
13 galvanitactic attraction; it simply means they're  
14 attracted by the electrical forces, actually exert a  
15 natural pulling on these cells in the wound bed.  
16 Application of exogenous or outside type electrical  
17 current then stimulates this natural attraction of  
18 cells towards an electrical charge.

19 In vitro studies done in various wound  
20 centers around the country have shown us that  
21 different cells that are involved in the healing  
22 process are actually attracted to a positive or a  
23 negative charge and that they differ in their  
24 preference for a negative or positive charge. For  
25 example, the anode, the positive electrode, actually

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1 attracts neutrophils and macrophages and in so doing,  
2 supports autolysis. Similarly, the epithelial cell  
3 also likes to or is attracted to the positive anode  
4 and this will help to support new epithelialization  
5 during the healing process.

6 The cathode attracts neutrophils and in so  
7 doing supports inflammation and fager cytolysis.  
8 Similarly, fibroblasts are attracted to the cathode,  
9 and this helps to support granulation tissue  
10 formation.

11 Now, this has implications when we look at  
12 a chronic wound and I promise you, I didn't bring the

worst one of the worst that I had. The case in point here, a wound that is clearly diffusely covered with devitalized tissue and what we would graphically see happening with electrical current being applied to such a wound is on the left of the illustration here, we see that the wound bed filled with a moistened saline gauze dressing and a positive electrode being applied here, and the electrode being placed in that conductive solution of saline is, being a positive electrode, will draw negatively charged neutrophils and macrophages into this area, and help to promote the autolysis of this necrotic tissue.

Similarly, if we look at a wound that is

beginning to fill with granulation tissue but still needs considerably more granulation matrix to complete the healing process, would be supported by the application of a negative electrode that would promote the attraction of the fibroblast into the wounded area and therefore enhance the laying down of the protein matrix in the wound bed.

Now that's kind of a brief overview of how is it that this electrical current actually promotes the growth of new tissue in a wound bed, what activity it engages in in terms of attracting the very cells that are essential to the normal healing process as we know it.

I would like to turn attention briefly to how is it that we deliver electrical stimulation and I'm aware that all of you got a huge packet of materials, as did I, so this will be brief, because I know you have read many of the papers that describe these different types of stimulation.

Basically there are what I believe are four types that have really been used, at least to some extent with wound healing, and these are them. The low intensity direct current, the high voltage pulse current, actually two forms of alternating current, the low voltage pulse microamperage current,

and then TENS.

You do see an occasional reference to the use of electromagnetic energy, pulsed electromagnetic

4 energy. This is actually using electromagnetic  
5 fields, it is different than electrical stimulation,  
6 which is using current. And so I have sort of set  
7 that aside as sort of a different modality than is  
8 electrical stimulation.

9 There is also some reference to using  
10 spinal cord stimulation, but most of that work is  
11 involved using it for chronic pain control and  
12 therefore, I am also setting it aside as a type of  
13 modality for chronic wound healing.

14 Of these four types then that have been  
15 most extensively addressed in the literature on wound  
16 healing, they differ in the characteristics of the  
17 actual current that's delivered, and I will just  
18 briefly highlight those for you. It's helpful when I  
19 was first learning all of this area of science, it  
20 was always helpful to me to be able to look at these  
21 diagrams, so I will share them with you.

22 The low intensity direct current which you  
23 see illustrated here is actually a continuous  
24 monophasic wave form, as you can see, and it's  
25 delivered using anywhere from around 20 to 200

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1 microamps of current at a very low voltage, only  
2 about, less than eight volts of current. This has  
3 been used more in the early work on electrical stim  
4 and wound healing, and more recently one does not see  
5 as much use of the direct current, in part because of  
6 problems with heat build up under the electrode when  
7 it is used.

8 Now high voltage pulse current as you see  
9 depicted here is short pairs of pulses with a long  
10 duration or pause in between, and this is delivered  
11 at 75 to 200 volts, and 80 to 100 pulses per second,  
12 and provides a total current of about 2.5 microamps  
13 when we use a standard electrode. Both the high  
14 voltage and the low voltage are capable of being  
15 delivered with either the positive or the negative  
16 electrode as the active electrode. This is the type  
17 of current you see used in some of the more recent  
18 research studies that you had the opportunity to  
19 review.

20 Alternating current is basically a

21 symmetrical biphasic pulse that uses a low voltage  
22 milliamperage and as you can see, it's biphasic and  
23 so the amount of charge in the two symmetrical phases  
24 of the wave form is equal, and consequently, there is  
25 no charge left in the tissue, it basically cancels

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1 each other out.

2 And then a similar type of wave form is  
3 seen in what is more commonly referred to as TENS,  
4 it's technically low voltage pulse milliamperage  
5 current. This also is a type of alternating current,  
6 as you can tell by the wave form. It delivers  
7 anywhere from 15 to 20 milliamps of current at 150  
8 milliseconds pulse width and a standard low frequency  
9 of 85 hertz.

10 Now, the real question is, well, you've  
11 got all these different kinds of current, what  
12 difference is there between them and does it really  
13 make any difference when it comes to wound healing.  
14 And the question is not one that is easily answered.  
15 In an attempt to try to address this question as well  
16 as a few others in this area of electrical stim and  
17 wound healing, one of my doctoral students and I,  
18 along with the assistance of a statistician at the  
19 University of Iowa, recently published a  
20 meta-analysis, which I believe you've also had a  
21 chance to review, and in that meta-analysis we looked  
22 at 15 studies that were judged to be amenable to a  
23 meta-analysis.

24 And in those 15 studies, there were 24  
25 samples that received some form of electrical

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1 stimulation and there were 15 that got a control,  
2 most often a placebo but not always. What we found  
3 when we looked at the different types of current, was  
4 that in the case of TENS, and let me go to TENS, that  
5 in the case of TENS, the net increase in the rate of  
6 healing was just under 11 percent, 10.9 percent, the  
7 net increase in the rate of healing over a control.

8 In the case of the direct current, we had  
9 a net increase of 12.6 percent and then in the case  
10 of the pulse current, we had a net increase of 15.5  
11 percent. Now, the problem here was that there was a

lot of overlap in the confidence intervals and so consequently, the observed differences, it's difficult to determine whether the observed differences were in fact just a function of sampling error, and the small sample sizes that are in most of these studies contribute to that issue of sampling error.

Furthermore, these devices often were confounded by the fact that some of the devices tended to be used only with one type of wound. For example, the TENS, which you see here, tended to be predominantly used on pressure ulcers. Well, when you look at the control group ulcers, you find that the pressure ulcers were the type of ulcers that

healed more slowly, and so consequently, the rate of healing that was estimated for TENS may actually have been suppressed somewhat because of the lower rate of healing that was occurring in that type of wound that was most often used to test that type of device. So to say that one of these devices is more effective in healing than the other, that still appears from this data analysis to be an unresolved issue.

Similarly, the question arises about to what extent does the etiology of the chronic wound influence the effect of the electrical stimulation on healing, and the wounds that come to mind when we think of chronic wound healing are of course the pressure ulcer, which you see here, the venous stasis ulcer. Other types of chronic wounds include the arterial ulcer and also the neuropathic ulcer, otherwise sometimes referred to as the diabetic foot ulcer.

Now, what we find when we look at a meta-analysis of these data from these 15 studies is that the predominant type of wound that was looked at when studies addressed only one type of wound in their sample, the type of wound that was most often used was the pressure ulcer; that was in seven studies. Venous ulcers were identified as a single

type of wound in only two. The remaining six out of the 15 that were looked at in this meta-analysis were



3 a mix, and this mix consisted of a mix of pressure  
4 ulcers, other types of ischemic wounds, as well as  
5 some nonhealing surgical type wounds, wounds that  
6 had, were healing by secondary intention. There were  
7 no studies of diabetic foot ulcers and there are no  
8 studies of arterial ulcers, specifically isolating  
9 them as the type of wound selected for the sample.

10 With that in mind, the highest net rate in  
11 healing rate between the E-stim and the treated  
12 wounds and those that received a control, the biggest  
13 net increase was with pressure ulcers and that was  
14 13.3 percent per week. And in this sample, in these  
15 samples, there was not any overlap in the confidence  
16 interval, which suggests that the sampling error was  
17 not a major contributor to the difference between the  
18 E-stim group and the control groups in those samples,  
19 but the lack of adequate study sample that are  
20 specific to a type of chronic wound other than  
21 pressure ulcers causes us to have difficulty forming  
22 any kind of conclusions about the effectiveness of  
23 electrical stim in healing other types of chronic  
24 wounds. And this is an unfortunate gap in our  
25 research literature at this point in time.

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1 So then we're left with the question,  
2 well, to what extent does the etiology of the chronic  
3 wound, the cause of it, actually influence the effect  
4 that E-stim would have on healing? And at this point  
5 in our understanding of the repair process after  
6 injury, what we know is that the normal healing  
7 process is mediated by specific cells, and you see  
8 those diagrammatically illustrated here, and of  
9 course I have referred to them several times this  
10 morning. The inflammatory process mediated by  
11 lymphocytes and macrophages, the proliferative phase  
12 mediated by the fibroblast, and then of course  
13 remodeling, and this normal process is very much a  
14 function of these cells that come to the wounded area  
15 at the time of injury, and these cells play a  
16 strategic role in the process of repairing the tissue  
17 and regenerating new epithelial cells.

18 Now, we know that there is an attraction  
19 of these cells to a wounded area when electrical

20 current is put to the wound bed. It would follow  
21 that if there is adequate circulation to the wound  
22 and there are adequate substrates in that  
23 circulation, that the stimulation of the wound such  
24 that it provides an attraction of these cells to the  
25 wound bed would lead to an improvement in healing,

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1 but those are suppositions I'm making. I do not  
2 have, nor does anyone at this point in time have data  
3 to tell us whether the stimulation with electrical  
4 stim will augment healing in wounds other than  
5 pressure ulcers. The data is simply not there.

6 I would be happy to take questions at this  
7 time, or clarify any of the points that I made.

8 DR. ZENDLE: Question. At the beginning  
9 of your talk, you talked about the difference between  
10 the positive and negative in attracting the different  
11 kinds of cells.

12 DR. FRANTZ: Yes.

13 DR. ZENDLE: How does that, and again,  
14 this is sort of basic science here, but how does that  
15 play into the direct versus alternating current going  
16 back and forth between positive and negative?

17 DR. FRANTZ: Well, you know, that's an  
18 interesting question. There's been a lot of, some  
19 speculation in the scientific community about how  
20 actually does, like an alternating current work. And  
21 I actually have done my research mostly with  
22 alternating current and although I have seen an  
23 effect size from alternating current, when I look at  
24 the research on TENS, the small number of studies  
25 that there are, the effect size is not as great as it

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1 is when you look at the effect with like the high  
2 voltage pulse current. But when we did the analysis  
3 using meta-analysis we actually couldn't compute an  
4 effect size because the unfortunate way in which many  
5 of these studies were reported, they didn't give us a  
6 standard deviation or variance, so we couldn't  
7 compute a true effect size from a statistical  
8 standpoint.

9 And from a basic science perspective, I am  
10 not able to explain and I don't know that anyone else

11 can, I would certainly welcome anyone in the audience  
12 helping us on this, why if you give an alternating  
13 current, then you're getting both positive and  
14 negative in an alternating fashion, you would get any  
15 kind of attraction of cells, because it's the  
16 polarity that brings the cells. I am not able to  
17 give you an answer to that, I do not know.

18 DR. ZENDLE: Sort of a follow-up question  
19 then is, if the basic science theory is that positive  
20 or negative attracts certain kinds of cells, does the  
21 opposite repel them?

22 DR. FRANTZ: I don't know, I have never  
23 thought about that. That's a good question. It  
24 possibly could. I don't know the answer. Yes?

25 DR. STANTON: You classified Pulstar F as

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1 different from the others, and I understand  
2 physically why you would, but I think since we're  
3 going to consider that with these other therapies.  
4 Can you make some comments about potential  
5 physiologic mechanisms, how they might differ from  
6 the more electrical stimulation and you know, just  
7 what your general opinion is.

8 DR. FRANTZ: The pulsed magnetic fields,  
9 the feeling is that those magnetic fields are again,  
10 drawing cells into the wounded area. The research on  
11 the electromagnetic field has been more limited,  
12 particularly in the human wound. Most of the work  
13 has been done in the animal model; you may be aware  
14 of many of those studies. And they don't provide us  
15 with much information then about what this  
16 electromagnetic field might do in a chronic wound,  
17 which is different than you can get in an animal  
18 model where we don't really have a good model of a  
19 chronic wound. But the electromagnetic energy is  
20 felt to increase blood flow to the area, some of the  
21 same kinds of things that happen with electrical  
22 stimulation.

23 DR. OLECK: Question. In terms of the  
24 categorization of the different types of devices, you  
25 talked about the high voltage pulse current, and I

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1 was looking at the ECRI report and some of the other

2 things, and it looked like there was another  
3 category, a low voltage pulse current. Am I missing  
4 something there, or are they basically dividing  
5 things up into pulsed current into two different  
6 groups?

7 DR. FRANTZ: It's interesting how we all  
8 have our different sort of categories. They  
9 identified direct current, pulse direct current,  
10 which is what I called high voltage pulsed current.  
11 I'm looking at a table that was included in the  
12 memorandum to the Medical and Surgical Procedures  
13 Panel, dated September 25th, 2000.

14 DR. OLECK: I was looking at their main  
15 document where they talked about pulse current  
16 applications and they distinguished between two  
17 subcategories, pulse direct current and high voltage  
18 pulse current, and I looked at the table where they  
19 had compared the studies of a number of those, and  
20 what they put in the pulse direct current had low  
21 voltages, like 6 to 12 volts, as opposed to this 75  
22 to 200.

23 DR. FRANTZ: Well, right. And when you  
24 do, with pulsed current, because you have, you're  
25 only giving the charge with the pulse and then there

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1 is that long interlude of space, then the actual  
2 voltage is higher, that's delivered with the pulse,  
3 but the total accumulation of current in the tissue  
4 is not different.

5 DR. OLECK: So you're saying in your view  
6 at least, that all of the pulsed current devices can  
7 be lumped together.

8 DR. FRANTZ: Basically are delivering the  
9 same kind or charge to the tissue.

10 DR. OLECK: Thank you.

11 DR. SIGSBEE: A quick question. What was  
12 the magnitude of the resting potential at cross scan,  
13 was that microamps or milliamps?

14 DR. FRANTZ: I have to look again. It is  
15 millivolts.

16 DR. SIGSBEE: Millivolts?

17 DR. FRANTZ: Yeah. And it averages -- I  
18 mean all those numbers I had on those figures, which

19 is from Folz and Barker's work, if you take the  
20 average of them, it comes to about minus 23  
21 millivolts. Other things?

22 MS. CONRAD: Dr. Frantz, would you give us  
23 for the record a little summary of your credentials?

24 DR. FRANTZ: Yes, I will be happy to, and  
25 I didn't even think about the fact that you wouldn't

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1 probably know them. I am a professor of nursing at  
2 the University of Iowa. I have my Ph.D. And my  
3 research is over the last 12 or 15 years, has focused  
4 in the area of wound care. I have had two NIH funded  
5 studies to address the effects of electrical stim,  
6 specifically TENS, on wound healing, and the subject  
7 pool that I used for those studies was predominantly  
8 elderly patients, many of whom are in nursing homes.

9 And my involvement in electrical stim  
10 really came out of my clinical practice as a nurse in  
11 intensive care units some years ago when I came to  
12 the realization that chronic wounds, in particular  
13 the pressure ulcer, occurred with some frequency and  
14 people didn't seem to have any good way to help them  
15 get healed. There was all sorts of various ways that  
16 people were treating them, but nothing seemed to be  
17 very effective. And I went to the literature in  
18 search of some better ideas, some better methods,  
19 came across some work being done on actually bone  
20 healing, that I'm sure many of you are familiar with,  
21 that showed some extremely positive benefits in the  
22 area of healing of bone with electrical current.

23 Coincidentally, a colleague of mine was  
24 studying pain control using the TENS to control pain  
25 and she was doing a study where they were looking at

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1 pain in donor sites, and some of the patients were  
2 getting a placebo TENS, others were getting  
3 electrical current with the transcutaneous electrical  
4 nerve stimulator, and much to their surprise, totally  
5 serendipitously, they were finding that the donor  
6 sites at the end of the studies, the donor sites that  
7 got the electrical stim had healed so much faster,  
8 and these were, you know, these were clean donor  
9 sites. These wounds had healed so much faster than

10 the wounds that were not treated, that got an  
11 inactive electrode.

12 And that sort of spurred my interest in  
13 the use of electrical stim, so I sort of came into it  
14 via the back door, but I have obviously spent a  
15 considerable number of years looking at this modality  
16 as an adjunctive treatment, if you will.

17 MS. CONRAD: Thank you very much.

18 DR. FRANTZ: You're welcome. Is there any  
19 other questions? Thank you very much.

20 MS. CONRAD: We will now have the  
21 presentation of the questions to the panelists,  
22 presented by Lorrie Ballantine and Perry Bridger.

23 MS. BALLANTINE: Good morning, ladies and  
24 gentlemen of the panel, and thank you for coming  
25 together to review another issue for us. The issue

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1 we are bringing before you today is electrical  
2 stimulation for the treatment of chronic wounds.

3 Chronic wounds are a significant problem  
4 for the Medicare population, with considerable  
5 morbidity and mortality. Treatment of wounds costs  
6 the Medicare program over \$3 billion a year.

7 For our discussion today, we are looking  
8 at three types of chronic wounds, pressure, venous  
9 and arterial. Pressure ulcers, the most common type,  
10 also known as decubitus ulcers or bed sores, affects  
11 3 to 14 percent of hospitalized patients and 15 to 25  
12 percent of residents in skilled nursing facilities.  
13 Venous ulcers are primarily caused by venous  
14 hypertension. 1.3 million patients are treated  
15 annually for these types of ulcers. The third type  
16 of ulcer is arterial, which often occur in patients  
17 with peripheral vascular occlusive disease or other  
18 clinical condition that has ischemia as an underlying  
19 etiology.

20 Although there is consensus on what  
21 constitutes conventional therapy, debridement,  
22 cleansing, dressing and nutrition, we do not know the  
23 precise role of adjunctive therapies such as the use  
24 of electrical stimulation. In keeping with the  
25 recommendations from the MCAC Executive Committee, we

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1 are posing two basic questions to you today. You may  
2 want to refer to the questions in your packet that  
3 you received today.

4 The first question for you to answer, is  
5 the evidence adequate to draw conclusions about the  
6 effectiveness of electrical stimulation as an  
7 adjunctive therapy for chronic pressure ulcers? In  
8 answering this question the panel should consider the  
9 following points: The adequacy of the individual  
10 study design; the consistency of results across  
11 studies; their applicability to the Medicare  
12 population; and the generalizability beyond the  
13 research setting.

14 We ask that you consider the whole  
15 spectrum of information presented, which includes  
16 expert testimony and public comments, to reach your  
17 conclusions on the adequacy of the evidence. Then if  
18 you feel the adequacy of the evidence is sufficient,  
19 we ask that you determine the size and direction of  
20 the effectiveness.

21 Again keeping with the Executive Committee  
22 recommendations, there are seven categories of  
23 effectiveness attached to the questions. Is the  
24 effectiveness a breakthrough technology, more  
25 effective, as effective with advantages, as effective

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1 with no advantages, less effective with advantages,  
2 less effective with no advantages, not effective. We  
3 ask that you break down your decisions and answer  
4 each question for all indications identified, chronic  
5 pressure ulcers, chronic venous ulcers, chronic  
6 arterial ulcers.

7 Also presented in your information and as  
8 Dr. Frantz had mentioned, you will find there are  
9 several types of electrical stimulation. Direct  
10 current, pulse current, alternating current, pulse  
11 electromagnetic field, transcutaneous electrical  
12 nerve stimulation, pulse electrical energy. In the  
13 technology assessment they have varying conclusions  
14 based on indications and type of electrical  
15 stimulation. Although we did not choose to  
16 explicitly ask you 18 separate questions, you may  
17 wish to separate your final panel recommendations by

18 indication and type of stimulation.

19 Thank you for your time, and we look  
20 forward to today's meeting.

21 MS. CONRAD: Thank you, Lorrie. Okay.  
22 Let's do a little summary of coverage history. John  
23 Whyte.

24 DR. WHYTE: Thank you, Connie. Good  
25 morning, Dr. Garber and Dr. Maves, as well as other

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1 members of the panel and public. Over the next ten  
2 minutes I am going to provide a general background on  
3 the history of Medicare coverage relating to  
4 electrical stimulation for the treatment of chronic  
5 wounds, as well as discuss why we sent this topic to  
6 your panel.

7 You've all received a background memo in  
8 your packet prior to the meeting, a memo dated  
9 September 25th, and I'm basically going to go over  
10 that document. You might want to take out the rest  
11 of your packet, which includes the technology  
12 assessment, several letters, the AHCPR clinical  
13 practice guidelines for the treatment of pressure  
14 ulcers, the literature review prepared by HCFA staff,  
15 and a bibliography.

16 I will first discuss the status of  
17 coverage before the technology assessment. You will  
18 then hear a presentation on the technology assessment  
19 and then finally, I will update you on the activities  
20 that have transpired since the assessment.

21 Now the coverage process dates back  
22 essentially to the 1970s, when Medicare contractors  
23 reimbursed for some forms of electrical stimulation  
24 for wound healing on a case by case basis, but  
25 essentially there was no national coverage policy in

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1 place. Now in 1981, HCFA did issue a national  
2 noncoverage policy for low intensity direct current  
3 in treatment of pressure ulcers. There is no  
4 additional activity until 1994, when the Agency for  
5 Health Care Policy and Research, AHCPR, which is now  
6 known as AHRQ, convened an independent panel of  
7 experts who produced a clinical practice guideline  
8 entitled Guideline on the Treatment of Pressure



9       Ulcers, and you all have that as part of your packet,  
10       and you may wish to refer during your deliberations  
11       to pages 8, 19 and 55, for some of the comments on  
12       electrical stimulation.

13               Specifically in a section on adjunctive  
14       therapy, the guideline advised physicians, "To  
15       consider a course of treatment with electrical  
16       therapy for stage III and stage IV pressure ulcers  
17       that have proven unresponsive to conventional  
18       therapy. Electrical stimulation may also be useful  
19       for recalcitrant stage II ulcers." The guideline  
20       states that the recommendation was based on data from  
21       five clinical trials involving a total of 147  
22       patients, and AHCPR assigned this portion of the  
23       evidence a strength of evidence of level B. AHCPR  
24       defines strength of evidence as level B if there is  
25       fair research based evidence to support the

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1       guideline. Level A is good research based, and Level  
2       C is expert opinion. And more information on how  
3       AHCPR defines strength of evidence can be found on  
4       page 18 of the guideline.

5               Now in 1995 in an effort to gain greater  
6       clarity on this topic, HCFA ordered a technology  
7       assessment of electrical stimulation, and ECRI, a  
8       technology assessment firm in Plymouth Meeting,  
9       Pennsylvania, was awarded the contract. And I think  
10       ECRI just arrived with Dr. Lerner and Dr. Turkelson,  
11       and at this point of the presentation I am going to  
12       defer to Dr. Charles Turkelson of ECRI, who will  
13       present the assessment, and you should all have  
14       copies of his slides in your materials.

15               After Dr. Turkelson presents the  
16       assessment, you may wish to ask questions then, or  
17       you may wish to hold your questions, it's completely  
18       up to you, because I will update you as I mentioned  
19       earlier, on what transpired at HCFA since the  
20       technology assessment. So first, Dr. Lerner.

21               DR. LERNER: Actually, just before my  
22       colleague starts, I'm Jeff Lerner, ECRI. Let me just  
23       introduce what Charlie is going to talk to you about.  
24       Charles Turkelson is our chief research analyst.  
25       ECRI is a nonprofit health services research

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1 organization, it's often compared to Consumer  
2 Reports, it is very independent in its views and it  
3 is designated as an evidence based practice center by  
4 the Agency for Health Care Research and Quality.

5 What Charlie is going to present to you is  
6 the results of our report, but also how to understand  
7 our report. He has a three-part presentation that  
8 looks at what basically is an evidence report, what  
9 statistics do you need to know to understand this  
10 very complex data set that is in the report, and then  
11 finally, how this report applies to the questions  
12 that you have in front of you. And I can't stress  
13 heavily enough that it really is a complex data set.  
14 Then at the end, if you'd like, we can talk to you  
15 about some next steps that we think would be valuable  
16 to take up in terms of research. So, Charles  
17 Turkelson.

18 (Pause while equipment set up.)

19 DR. TURKELSON: I do apologize for that  
20 delay. I want to express my gratitude for having the  
21 opportunity to speak before you for several reasons,  
22 first, is that it actually gives me a chance to  
23 explain the difference between say a technology  
24 assessment and hard evidence report, and other kinds  
25 of documents. This is a difference that is widely

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1 unappreciated. If I am saying something that you  
2 already know, I apologize for that, but given the  
3 commonality of the failure to make a distinction  
4 between a technology assessment report and some other  
5 kind of document, I would like to begin with that.

6 And the obvious thing is that it is not a  
7 guideline. The primary purpose of this report as in  
8 any evidence report, is to synthesize evidence.  
9 Evidence is defined as that which comes from clinical  
10 trials. An evidence report does not use a consensus  
11 process, they do not incorporate opinions, they  
12 merely try and state whether available evidence shows  
13 whether available evidence shows whether available  
14 evidence shows whether a technology works, if you  
15 will allow me to put that in quotes.

16 The ramification of that is the other oft

misunderstood phrase, and that's the phrase no evidence. No evidence means no evidence. It means that an evidence-based conclusion cannot be drawn. It does not mean that a technology is not effective. I will state it another way to emphasize the report, the absence of evidence of effectiveness is not evidence of no effectiveness. In a technology assessment or evidence report, we strive to stay very close to the data and when there are no data, there

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1 is very little for us to say.

2           As such, these reports do not make  
3 practice recommendations and they do not make  
4 coverage decisions. Both of those often involve  
5 clinical judgment. Again, these kinds of reports  
6 look at data, they do not incorporate opinion. In a  
7 practice recommendation or a coverage recommendation,  
8 you often times need to consider clinical opinion;  
9 this is beyond the purview of such a report.

10           I want to turn now to the next section of  
11 my talk, which is how to understand this report.  
12 Where we are headed in all of this is that in  
13 general, there is evidence for the efficacy of  
14 electrical stimulation, but, and that's a very big  
15 but, in general has limited meaning here because this  
16 is a complex data set, although it's comprised of  
17 only eight or nine studies depending on how you  
18 count. It is a very complex data set. And I need to  
19 walk you through the logic of this report so that you  
20 can see why the data set is so complex. And I am  
21 going to take a hypothetical evidence table here  
22 which shows the result of five studies, three of  
23 which are significant and two of which are not, and  
24 the temptation here may be to say that the results of  
25 these studies are different, that these studies are

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1 not consistent in their results.

2           The temptation may further to be to say  
3 that indeed, this vote between the studies is mixed,  
4 that well, it's an odd number of studies, either the  
5 yeses or nos have to win. We really don't -- had  
6 there been a sixth study it may be a tie, and we're  
7 not capable of coming to a decision.

8 We can show another version of this  
9 evidence table by now presenting the p-values, the  
10 results of the test of statistical significance, and  
11 there we see that two trials are again  
12 nonsignificant, and Study 5, for instance, finds a  
13 miniscule trial, and the temptation in looking at  
14 those kinds of results is to say that my goodness,  
15 Study 5 found a huge effect where study 1 found  
16 almost no effect whatsoever. Unfortunately, that  
17 interpretation of the literature is utterly wrong.  
18 And to understand why it's wrong requires some  
19 understanding of the t-test and the formula for the  
20 t-test that I put up here is not as imposing as it  
21 looks. There are just a couple of things you need to  
22 know about it, first of all, if the value of t  
23 increases, the more likely it is you're going to get  
24 statistical significance. A big t means a low p  
25 value with statistical significance. A t around 1

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1 means it's nonsignificant.

2 But the most important point I want to  
3 make on this formula is it has two terms, they're  
4 each denoted in brackets, one on the left and one on  
5 the right. The term on the left is an effect size;  
6 you can look at the numerator in the term there, the  
7  $X_{sub-e}$  and the  $X_{sub-c}$ , and see that that's the  
8 difference between the experimental and the control  
9 groups. So as your treatment becomes more effective,  
10 that difference between the experimental and the  
11 control groups will increase, and t will increase.  
12 But that is the only part of that formula that  
13 actually gives you the size of the effect, the  
14 magnitude of the effect. The p-values simply do not.  
15 But I do want to say that that concept of effect  
16 size, that left-hand term denoted here, I think is  
17 arguably the most important concept in research  
18 synthesis. It allows you to look at something and  
19 say how well it works, and as a matter of fact, that  
20 chunk of t-test that we'll be using in the  
21 meta-analysis that we present later is our measure of  
22 effect size.

23 If there are any statisticians in the  
24 group, that's known as the Hedges G or Hedges D, but

25 just think of it as a chunk of t-test, that piece

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1 that tells you how big the effect was.

2 Again, to restate the point in another  
3 way, if we rook at the right-hand term of the  
4 equation, it contains only the number of subjects in  
5 each group. And you can change the number of subject  
6 in each group, increase the value of t, and thereby  
7 increase the probability that you will get  
8 statistical significance. The t-value in other  
9 words, can be strictly related to just the number of  
10 subjects in a group, the number of patients in a  
11 group. The t-value and the p say nothing about the  
12 size of the effect. A p equal to .4 may actually be  
13 a bigger effect than a p equal to .0001, because it  
14 all depends on the number of subjects in a group.

15 And if you think back to those first  
16 slides, where I had two studies that were  
17 nonsignificant and three that were significant, and  
18 the subsequent slide where I had p-values, one at the  
19 bottom which was very small and one at the top which  
20 was relatively large, here's actually how I generated  
21 all of those p-values. The means in all of the  
22 groups were identical, the means in all of the  
23 control groups were identical, the means in the  
24 experimental groups were identical, the standard  
25 deviations in the control groups were identical, and

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1 the standard deviations in the control groups were  
2 identical, only the number of subjects differed.

3 I can't reinforce this concept of effect  
4 size too much. And lest you think that this is  
5 something peculiar to the t-test, it is not. All of  
6 statistics boils down to this simple formula.  
7 Anytime you test statistical significance, you are  
8 multiplying some effect size times some measure of  
9 study size. The reason you want to do a  
10 meta-analysis is to look at that measure of effect  
11 size. You want to ask not just did it work but how  
12 well did it work.

13 Basing decisions on p-values actually  
14 leads you to very conservative conclusions. Here's  
15 an example of a kind of plot you will be seeing

several times through this talk. You may be familiar with it, but this is a synthetic data set. The first five diamonds there show the effect size now, which is denotable along the X axis and the thinner lines denote the 95 percent confidence intervals. Each of those five trials is statistically nonsignificant, so if I were to look at the five individual results of these studies, I would say five trials, five nonsignificant results, clearly it doesn't work, this technology is ineffective. In point of fact, that's

wrong. In point of fact, when you combine these results, when you look at the effect sizes, there is indeed effectiveness to this hypothetical trial.

Now, another thing about the problem with significance levels else is that using significance levels prevents one from seeing true patterns in data and also creates false patterns in data. Let's look again at those original five studies. We had a false pattern in the data; we had two that were nonsignificant and three that were significant. Here is a plot of the effect sizes of those studies. As they should, all of the effect sizes are identical, and then the overall result of this hypothetical meta-analysis is shown at the bottom. In other words, those results and those evidence tables were perfectly consistent with each other. They were engineered to be perfectly consistent with each other.

What I want to argue here is that the meaning of statistical tests of individual studies, p-values in particular, is arguably the most overused and misinterpreted concept in research synthesis. They are of limited value. If you have one study at hand, they are valuable; if you have more than one they are probably not valuable. That is one of the

primary reasons we sought to do a meta-analysis. Another of the reasons we sought to do a meta-analysis was to look for patterns in data.

You can only see those patterns if you look at the effect sizes, and in looking at effect sizes, you are by nature, doing a meta-analysis.

7                   So let me turn now to the report itself.  
8 I do have to begin with a couple of caveats, and that  
9 is, it's about four and a half years old, the update  
10 in the report is about three and a half years old, so  
11 it is the case that newer information isn't  
12 addressed. And I'm going to try my best to answer  
13 the questions that are before you. The upshot of  
14 this talk is that I won't be able to do it probably  
15 in a complete fashion, but I will explain why.

16                  I do know you have a question before you  
17 on arterial ulcers. The report that we have, the  
18 ECRI report, is silent on arterial ulcers simply  
19 because there is insufficient evidence from which to  
20 draw a conclusion about them. That is a case where  
21 the absence of evidence should not be taken as  
22 evidence of no effectiveness; there's just simply no  
23 data, we are not going to comment.

24                  So what I'm going to talk about today is  
25 primarily venous and decubitus ulcers. What we have

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1 done in our meta-analysis first of all, is to take  
2 the results of the investigators as published and  
3 recompute them wherever possible. The primary reason  
4 is because there are some problems ranging from  
5 moderate to serious with the outcomes that are  
6 reported in many of the clinical trials. One of the  
7 outcomes they reported is percentage of patients  
8 healed. That is plausible that if you are comparing  
9 two groups of patient, one as an experimental group  
10 and one as a control group, and the sizes of the  
11 ulcers at the beginnings of the studies are  
12 different, it's plausible that more patients will  
13 have completely healed ulcers if they begin with  
14 smaller ulcers.

15                  I know that these trials are randomized,  
16 but these trials are small randomized control trials,  
17 many less than -- several of them have less than ten  
18 patients. It's very difficult to guarantee that the  
19 wound sizes are identical, are near identical in the  
20 control trials with experimental and control groups  
21 of such small trials, and that is yet another reason  
22 for not wanting to use the percentage of patients  
23 healed.

24 (Technical problem delay.)  
25 For some reason I have some slides that  
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1 have died on me here in Power Point. I do want to  
2 comment on the quality of the literature. In  
3 general, it is the case that the clinical literature  
4 as you probably know, is not a perfect literature.  
5 The trials we're looking at are essentially nine  
6 trials, and if you look at the handout I gave you,  
7 they are listed on the slide entitled Primary  
8 Studies, and that should be on page 10. And it's  
9 those nine trials that comprise the bulk of our  
10 conclusions here.

11 Of these, seven were randomized, and of  
12 those seven, four were blinded. All but one trial  
13 specified that its controls received a sham device  
14 plus additional treatment. In five of the eight  
15 trials, this additional treatment was saline soaked  
16 gauze. In the electrical stimulation group, those  
17 patients received electrical stimulation plus this  
18 additional treatment, again, in five of the eight  
19 trials, the additional treatment was saline soaked  
20 gauze. This doesn't guarantee -- this is not a bad  
21 quality literature, I will say that. In looking at  
22 this literature, we compared it for instance to the  
23 quality of the literature on occlusive and  
24 nonocclusive dressings; it is of the same quality.

25 We also looked at it in a quantitative  
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1 fashion, because we did something that is fairly  
2 radical for a meta-analysis, and that is, we included  
3 uncontrolled trials in our analysis. But what we  
4 sought to do was determine whether the results of --  
5 not uncontrolled, unblinded trials and nonrandomized  
6 trials in our analysis. What we sought to do is  
7 determine if the result of the nonrandomized trials  
8 and the nonblinded trials were in fact different from  
9 those that were randomized and/or blinded. And in  
10 fact, those results were not different. The argument  
11 here is that we can use those trials because it  
12 doesn't make a difference if it doesn't make a  
13 difference.

14 Now there's a tremendous advantage to that



15 approach. The typical approach is to say if the  
16 trial is not randomized and it is not blinded, I am  
17 going to discard it. What that typical approach  
18 means is that there is nothing of interest to me in  
19 any of those trials. Stated another way, those  
20 nonrandomized nonblinded trials contain no  
21 information whatsoever. Well, I'm not convinced that  
22 that's true. As a matter of fact, these trials  
23 probably do contain some information, and that is  
24 certainly one of the reasons we incorporate these  
25 trials in this analysis.

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1 And again, we verified the fact that we  
2 could do so by testing whether including these  
3 trials, whether the lack of randomization and whether  
4 the lack of blinding would influence our results, and  
5 in fact it didn't. So we are allowed now to use the  
6 information these trials contain about wound healing,  
7 about rates of wound healing, about ulcer size, about  
8 the types of device they used, and so on, in  
9 considering the results of this analysis.

10 I know too you were asked a question about  
11 whether the results of these studies are consistent.  
12 In point of fact, they aren't. Here are the effect  
13 sizes for the nine trials. They are very different  
14 from each other. This is the basic fact one needs to  
15 grapple with when considering this literature, this  
16 is the core of the assessment, this is the key to  
17 thinking about this literature. This is not so much  
18 the result of the ECRI report or the ECRI analysis.  
19 This is what these investigators found. This is  
20 their effect sizes, we got to them by a simple little  
21 algebra. They are different, some of them very  
22 different. As a matter of fact, that's not bad.

23 One of the reasons for doing a  
24 meta-analysis is to explain the differences among  
25 trials. For those of you who are statisticians,

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1 philosophers or just obsessive compulsive, to be sure  
2 the kinds of result we get out are correlational,  
3 we're not getting causation, so we will say that such  
4 and such a thing correlates with better or worse  
5 wound healing, and not such and such thing causes

6 better or worse rates of wound healing. In point of  
7 fact, what we have here today is real decisions made  
8 by real people about real patients, and at least it  
9 is our opinion that having correlations is better  
10 than having no information at all. You can consider  
11 in your deliberations the meaning of correlational  
12 data, but you should at least be aware that these  
13 correlations exist.

14 Now immediately when trying to synthesize  
15 all nine trials, we ran into a problem. There was no  
16 combination of variables we could use to explain the  
17 differences among them. As a result, we did have to  
18 omit one study. The reason we omitted the study was  
19 because its reporting was a little poorer than some  
20 of the other studies. We would have liked a complete  
21 description of all studies, we didn't get such a  
22 complete description, so we had to discard this one.  
23 Now it turns out the study we discarded was a study  
24 by Salzberg et al. And it also turns out that this  
25 study found the largest effect, had the largest

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1 effect sizes of all trials. You can argue that a  
2 consequence of that is that our analysis is  
3 conservative, that it is biased, if you will, against  
4 finding an effect of electrical stimulation.

5 So we turned and looked again at the eight  
6 studies, again verified that the failure to randomize  
7 and the failure to blind had no effect on -- would  
8 have no effect on the results of our analysis, and  
9 again found an overall statistical significant  
10 effect, again found that there is still a lot of  
11 disagreement between the results, between the effect  
12 sizes of these trials, and found that the only way we  
13 could reconcile the differences among those trials  
14 was by looking at wound size, the type of ulcer, and  
15 how they were treated.

16 Now it turns out that smaller ulcers  
17 appear to heal faster in response to electrical  
18 stimulation than do the larger ones. It is possible,  
19 maybe even probable, that decubitus ulcers tend to  
20 heal better than venous ulcers. There is a caveat  
21 that that result may not be generalizable. There is  
22 some rather complex statistics we did in the

23 background that suggests that while this is a strong  
24 trend, there are some difficulties in generalizing  
25 this.

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1 Then the third thing that we need to  
2 explain the differences among these trials is the  
3 type of device, and that is, the ulcers that were  
4 treated with direct or pulsed current tended to heal  
5 less well than other forms of ulcers. Now real  
6 caveats are needed when talking about that. For  
7 statistical reasons we had to lump those two types of  
8 devices together, and we really cannot make  
9 conclusions about which individual device is best or  
10 which individual device is the worse, if you will.

11 Now overall, I want to qualify again, to  
12 arrive at those conclusions we had to discard the  
13 results of one trial. It does hinder our explanation  
14 of why these studies are different, why the effect  
15 size of these studies are different, and I want to  
16 keep coming back to that fact. The effect sizes in  
17 these studies are different. This is a thing the  
18 investigators found. To understand this data, one  
19 needs to understand why they are different. These  
20 are little small studies, which is somewhat  
21 problematic, even though they are randomized. I  
22 alluded to that problem before.

23 The meta-analysis we conducted partially  
24 gets around that fact, perhaps to a large part,  
25 although there are some technical criticisms that we

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1 bring out in the report that you could level against  
2 that meta-analysis. And I do want to stress that the  
3 literature is relatively good but not perfect. That  
4 I think is actually a strong positive statement about  
5 the quality of this literature. It is in general I  
6 think, there is another presentation I give about the  
7 quality of medical literature and the figure that I  
8 arrive at there is that 85 percent of all randomized  
9 control trials have the potential for very serious  
10 bias.

11 Again, I want to stress the fact that this  
12 data set is complicated. But I want to stress the  
13 fact too that if we just look at the simple

14 difference between the treated groups, those that  
15 received electrical stimulation plus typically saline  
16 soaked gauze, versus those that received typically  
17 but not always saline soaked gauze, there is a huge  
18 difference between the groups.

19 In terms of standard deviation units, it's  
20 1.1 standard deviation units. That's not a terribly  
21 easy figure for most people to grasp. Here's a  
22 picture and unfortunately the red doesn't show up, if  
23 you look at your slide, you'll see that the  
24 electrical stimulation graph is very far to the  
25 right. This I think tells a better story, and if we

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1 were to express these results as a two-by-two table,  
2 the improvement seen in the electrical stimulation is  
3 about three, in wound healing rates, is about three  
4 times higher than the improvement seen in the control  
5 groups. The difficulty is, those effect sizes are on  
6 average, and that with a data set like this, averages  
7 are very difficult to interpret.

8 Let's consider the following hypothetical  
9 treatment of ten studies. I have five studies on the  
10 left, where they show that this hypothetical  
11 treatment tends to kill patients; I have five studies  
12 on the right that show that this hypothetical  
13 treatment tends to cure patients. The average effect  
14 here is zero, no effect on average. That doesn't  
15 give us a whole lot of information. In fact, there  
16 are clearly some patients to whom you want to give  
17 this therapy and clearly some patients to whom you do  
18 not want to give this therapy. Thinking of that  
19 slide in terms of averages simply isn't useful.

20 We are in an analogous situation with the  
21 wound healing data. The information found by the  
22 investigators, the effect sizes found by these  
23 investigators are quite different from each other.  
24 It is partly for that reason that I really cannot  
25 address one of the questions that you have before

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1 you. And that is, to assess the effectiveness, the  
2 absolute effectiveness of the healing of venous  
3 ulcers versus the healing of decubitus ulcers. All  
4 we can do here is state it in relative terms. Again,

5 we are dealing with essentially eight studies, it's a  
6 very small data set for such complexity. But again,  
7 I want to stress the notion that the only explanation  
8 we could come up with are that the data are  
9 consistent with the idea that electrical stimulation  
10 is more effective on smaller perhaps decubitus ulcers  
11 and ulcers not treated with direct or pulse current.  
12 And in fact in those cases, the effects may be large.

13 The unfortunate situation here is that  
14 this is not a simple data set and that there are  
15 really no simpler conclusions I can offer you today.

16 With that having been said, I think I will  
17 just close the presentation here and open the floor  
18 to questions, if I may.

19 DR. GARBER: Let me just ask you a quick  
20 question for information. When you say you eliminate  
21 this Salzberg study because you could not explain the  
22 differences, could you elaborate on what you meant by  
23 being able to explain?

24 DR. TURKELSON: These studies find  
25 different effect sizes. Study A finds a huge effect,

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1 study B finds a very small effect. These effect  
2 sizes, if you do a statistical test, are  
3 significantly different from each other. What that  
4 means is that something else is going on in these  
5 trials besides electrical stimulation, something in  
6 addition to electrical stimulation is affecting these  
7 results. We eliminate the Salzberg trial because of  
8 its poor reporting, or I should say, less than  
9 complete reporting. That probably isn't a bad thing.  
10 Because it happened to have the biggest effect size,  
11 you can argue again that our analysis is a tad  
12 conservative. We didn't --

13 DR. GARBER: Well, I can understand  
14 eliminating the study because of some serious flaw in  
15 the study design, including poor reporting, but  
16 that's independent of the issue of whether its  
17 results were different.

18 DR. TURKELSON: We can't explain it. We  
19 cannot explain -- that is, as we state in the report,  
20 that's the difficulty in interpreting this analysis,  
21 given that there is no reason we could explain the

22 differences among all nine trials. Now, that is  
23 probably not a weakness of the analysis so much as it  
24 is a problem with less than complete reporting.  
25 Again, that's a very common thing in the medical  
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1 literature; I don't want to -- it's very easy for me  
2 to stand up and make it look like I'm picking on the  
3 electrical stimulation literature. In point of fact,  
4 I'm not. I'm picking on, I am trying to  
5 indiscriminately offend all the entire body of  
6 clinical research.

7 DR. GARBER: Can you, and this is not  
8 something in your presentation, but in the report, a  
9 great deal of discussion is devoted to your measure  
10 of the healing rate data and how that affected the  
11 statistical significance of the results. Can you  
12 talk about what effects, can you summarize the basic  
13 impact of choosing data as the measure as opposed to  
14 some of the end points that were reported in the  
15 trials?

16 DR. TURKELSON: Yeah, and unfortunately  
17 those were the slides that went blank on me.  
18 Interpretation of the other end points as reported in  
19 the trials is a tad difficult. I think the easiest  
20 one to handle is some of these subjective rating  
21 scales, where the amount of exudate is measured or  
22 the amount of granulation is measured. In point of  
23 fact, I am not aware of research that addresses  
24 whether patients care about that. I would rather  
25 imagine they care about whether their wounds are

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1 healed. And that, we're really not doing anything  
2 novel here, that's just a standard procedure of  
3 taking a direct patient outcome over an intermediate  
4 patient outcome.

5 As far as healing rates go, again, those  
6 are dependent on the initial wound size, the size of  
7 the wounds at the beginning of the study. If the  
8 sizes in the experimental, of the wound sizes in the  
9 experimental and control groups at the beginning of  
10 the study are different, then healing rate or  
11 percentage of patients healed is terribly difficult  
12 to interpret. Because these are small randomized

13 trials, it's very easy to compromise the  
14 randomization schemes, and that's one reason we could  
15 look at it.

16 Then the wound healing rate is another we  
17 didn't look at, because the investigators tend to  
18 treat it as linear. It would seem to me that if  
19 wound healing rates have something to do with cell  
20 division, we have a case of one cell dividing into  
21 two, two dividing into four, four dividing into  
22 eight, and so on, which is a distinctly nonlinear  
23 process, and as a matter of fact, the exponential  
24 model that we used, the thetas, is consistent with  
25 the notion that cell division is exponential and not

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1 linear.

2 DR. GARBBER: Well, actually, that wasn't  
3 totally clear to me. If you think that -- somewhere  
4 in the report it said that the wounds are basically  
5 three dimensional, and you're measuring something  
6 linear typically for the healing rate, which is, I  
7 thought it was wound diameter or something like that.

8 DR. TURKELSON: Well, it is a three  
9 dimensional, and you're also, I'm sure if you read  
10 the report, are aware that this is a model we  
11 validated in the report as well. Not only is there a  
12 publication that addresses this fact, but every time  
13 somebody in one of the papers presented raw patient  
14 data, we went back and made sure that that followed  
15 an exponential model and every time we could attempt  
16 to validate the exponential rate, we were able to.  
17 There is certainly evidence then to suggest that is  
18 the way these wounds heal and there is an absence of  
19 data to suggest that they would heal linearly. I am  
20 not frankly aware of any general argument, but it is  
21 difficult to conceive of any biological process  
22 that's linear. Biology just doesn't work that way.

23 DR. GARBBER: No, we dont need to go off on  
24 this, the alternatives to linear. There's many other  
25 kinds of models.

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1 DR. TURKELSON: There's many other kinds.  
2 This equation seems to fit very well. And again,  
3 this isn't our idea, this isn't novel, this was a

4 notion that was published by Salzberg and again, we  
5 take his exponential model, all of the data we are  
6 able to get seemed to fit that model. Yes.

7 DR. OLECK: I have a question that focuses  
8 in on the variability of these devices. Again the  
9 report and looking through all the studies, it  
10 clearly indicated there were several different  
11 categories of devices?

12 DR. TURKELSON: That's correct.

13 DR. OLECK: And within each particular  
14 category, there were different types of devices and a  
15 very wide variety of settings within those. Can  
16 lumping all those of those things together trying to  
17 do this meta-analysis, to try to gain some  
18 significance? I guess I would like you to talk again  
19 about the appropriateness, the reasonableness of  
20 doing those with all those different technologies,  
21 and if we come to some conclusion based on putting  
22 together all of those technologies, then is that  
23 conclusion saying that well, any electrical device  
24 would fall into that same category? Why look at  
25 things over this broad range of devices rather than

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1 on at least a particular modality or particular type  
2 of device?

3 DR. TURKELSON: I'm not sure I understand  
4 your question, so if I'm not answering it, please  
5 interrupt me. I will begin by saying we have a  
6 partial answer. We did look individually by devices  
7 in the narrative section of the report. The  
8 difficulty is that there are probably too few trials  
9 of any given device to meta-analyze, so again, a  
10 nonmeta-analytic systematic narrative review, if you  
11 will, is inherently biased towards being  
12 conservative. Hark back to that one slide I showed  
13 with five trials that were, each of which had  
14 nonsignificant results, and then one trial that had  
15 statistically significant results. That's a  
16 manifestation of that bias.

17 So we tried to address the individual  
18 wound devices in a narrative review but felt we  
19 wanted more statistical power, felt we needed to be a  
20 little less biased toward the conservative, and



21 lumped these devices together. Now unfortunately,  
22 the only way you can do it is by lumping these two  
23 devices together in sort of a statistical construct  
24 category. I think the nice thing about that result  
25 is that it satisfies the statisticians and the lunks  
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1 like me. The bad thing about the result is it's very  
2 difficult to interpret.

3 We could come up with no manipulation of  
4 the variables that would explain the differences  
5 between these trials other than the ones we used.  
6 All I can tell you is that this construct that is  
7 comprised of these two devices, tends to get wound  
8 healing. This is I suppose one of those points where  
9 the stock answer, this is a complex problem in need  
10 of future research, is given. I can't offer you the  
11 answer I want because I don't have the data.

12 DR. OLECK: When you say two devices, I  
13 guess I was looking through, and in one of those  
14 primary studies, it looks like they fall into several  
15 different studies.

16 DR. TURKELSON: The primary studies do.  
17 What we did is, we divided the device types into two  
18 categories in general. The first category is  
19 comprised of those two devices, the AC device and one  
20 of the other, and then all of the other devices. It  
21 is a very difficult construct to interpret. The  
22 difficulty is that, the problem is that, we know that  
23 there's clearly something going on here, but we don't  
24 know how to explain it.

25 DR. STANTON: Let me build on something I  
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1 think Adrian was trying to get at. You and your  
2 colleagues I think have probably an exquisite  
3 understanding of these studies, and have probably  
4 discussed them and debated them and done some very  
5 sophisticated analysis on them.

6 DR. TURKELSON: I will say as of four and  
7 a half years ago, I did. Now we'll see.

8 DR. STANTON: What I would like you to do,  
9 which may be abhorrent to statisticians, is to give a  
10 qualitative perspective, because I think you have  
11 pointed out very nicely the problems with the

12 meta-analysis on here, and we could spend a day  
13 debating the meta-analysis and please, let's not.  
14 But if you could, it seems to me there's a reasonable  
15 body of literature here about decubitus ulcers and  
16 various type of electrical stimulation, if you could  
17 give a qualitative assessment of that. And then do  
18 the same for venous, which there seems to be almost a  
19 reasonable amount of literature on. And then lastly  
20 can you do it for arterial/diabetic and incorporate  
21 other studies that have come out since the report?

22 DR. TURKELSON: I cannot incorporate  
23 studies that have come out since the report.

24 DR. STANTON: Okay. You have not looked  
25 at anything?

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1 DR. TURKELSON: I have not looked at that.

2 DR. STANTON: Okay. Then just the first  
3 two, please.

4 DR. TURKELSON: Obviously, the report was  
5 silent on arterial, because at that time there was no  
6 data. The first two, the short answer to your  
7 question is no, I can't. We can't look at venous  
8 ulcers in isolation with this data set. We can't  
9 look at decubitus ulcers in isolation with this data  
10 set. We have to look at them relative to one  
11 another. It's a very complicated explanation, I  
12 know. Decubitus ulcers appear to heal faster than  
13 venous ulcers. Smaller ulcers appear to heal faster  
14 than larger ones. Ulcers treated with a certain type  
15 of device or devices appear to heal faster than  
16 ulcers treated with another kind of device.

17 So if I'm looking at say decubitus ulcers,  
18 I can't make the blanket statement because it  
19 depends, at least from this data set, on the initial  
20 size of that ulcer and the type of device used. I  
21 can't make a blanket statement about venous ulcers  
22 other than to say they appear to heal less fast than  
23 the decubitus, because again, the venous ulcers,  
24 their healing rates appear to depend on the initial  
25 size of the ulcer and the type of device used.

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1 That having been said, if we look at the  
2 positive, the small ulcers, the decubitus ulcers, it

3 would seem that there is something very large going  
4 on. If you recall that two-by-two table, where there  
5 is a 75 percent patients healed of patients treated  
6 and 25 that are not, that's a massive effect, and  
7 that's a massive effect that is an average, so that  
8 average can be dragged down by something, as well as  
9 pulled up. So somewhere buried in this data set is a  
10 big effect. I -- it's all the data will allow me to  
11 do. I wanted to harp on the complexity of the data  
12 because I can't give you exactly what you want.

13 DR. STANTON: Right. And I think one of  
14 the things that we're going to struggle with is  
15 trying to tease that out, and I don't think it's  
16 going to be reasonable to say, well, every device is  
17 going to have to go out there and do separate  
18 randomized control trial on every different type of  
19 ulcer subdivided into different sizes of ulcers.

20 DR. TURKELSON: Right.

21 DR. STANTON: I think it's just a  
22 difficult issue the panel is going to have to  
23 struggle with.

24 DR. TURKELSON: You're now seeing actually  
25 why I began the presentation with the difference

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1 between a technology assessment and say a coverage  
2 decision or a guideline. I can tell you what the  
3 data is, but I don't want to make those type of  
4 clinical judgments that you're going to have to make  
5 for this decision. These are the data, and I'm  
6 passing the problem on to you.

7 DR. GARBER: Charles, maybe I can just ask  
8 one more detail for your response to Marshall's  
9 question there, and it really has to do with  
10 distinguishing the venous ulcers from the decubitus  
11 ulcers.

12 DR. TURKELSON: Yes.

13 DR. GARBER: Now the studies as I  
14 understand it for the most part have mixes of these  
15 two. So can you elaborate -- we will have to  
16 eventually address questions you heard from before  
17 about each of these indications separately, and you  
18 stated that there is evidence of greater healing  
19 rates with the decubitus ulcers.

20 DR. TURKELSON: With the smaller decubitus  
21 ulcers.

22 DR. GARBBER: Okay. I would like you to  
23 just explain a little bit how you came up with that  
24 conclusion, given the mix of the two types of ulcers  
25 in the published studies.

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1 DR. TURKELSON: First of all, none of the  
2 studies we used had mixed patients. That was one of  
3 our inclusion criteria, so the studies we took all  
4 had, either used all decubitus or all venous.

5 DR. GARBBER: You mean within one case?

6 DR. TURKELSON: Within one trial.

7 DR. GARBBER: Okay.

8 DR. TURKELSON: None of these nine trials  
9 had an add mixture of patients with venous and  
10 decubitus ulcers.

11 The answer to the rest of your question is  
12 not so simple. It was essentially a metaregression  
13 that we performed. To fully answer it, I'd have  
14 to --

15 DR. GARBBER: That's okay. I mean, that's  
16 the equivalent of doing something like subgroup  
17 analysis on a pool study.

18 DR. TURKELSON: Yeah, but we were not  
19 dealing with heterogenous patient populations within  
20 a given trial.

21 DR. GARBBER: Right, okay. So you have  
22 separate trials, so you pooled separate -- you could  
23 in theory, you used regression analysis, but in  
24 theory you could have separately pooled the  
25 decubitus, the trials using decubitus ulcers and the

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1 trials using venous ulcers; correct?

2 DR. TURKELSON: In theory you could have.  
3 You'd lose information by doing that.

4 DR. GARBBER: I understand, and that's why  
5 you chose the regression analysis.

6 DR. TURKELSON: Yes.

7 DR. GARBBER: There's another way we can  
8 think of this, is that with regression analysis, we  
9 are mimicking what you might have done by pooling the  
10 two types of trials separately.

11 DR. TURKELSON: That's an approximation,  
12 yes.

13 DR. GARBER: Yes, understood, okay.

14 DR. TUNIS: Okay. Well, thanks, Dr.  
15 Turkelson, and thanks, Dr. Lerner, as well. Now  
16 Dr. Whyte is going to sort of update this for a  
17 little bit of filling in the information of what's  
18 happened since the report was put together, a little  
19 more background, and then we will go to break.

20 DR. WHYTE: As Dr. Turkelson mentioned,  
21 this report was done in 1996 and it is the year 2000,  
22 and sometimes we move slow but we don't move that  
23 slow, so I'm just going to spend the next few minutes  
24 updating on you what we have done since your report  
25 was completed.

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1 When the report was completed in 1996,  
2 HCFA referred the topic to the technical advisory  
3 committee, and at that time the TAC consisted of  
4 government physicians and HCFA contracted medical  
5 directors. The TAC reviewed the ECRI report and they  
6 noted that wound healing outcomes in many of these  
7 studies may have compromised by several confounding  
8 factors, and therefore, they voted to issue a  
9 noncoverage recommendation.

10 Dr. Turkelson briefly mentioned how in  
11 1997, ECRI prepared an update of its original report  
12 and you also have that as part of your packet. Now  
13 based on the update as well as the TAC  
14 recommendation, HCFA rescinded carrier discretion --  
15 remember, previous to that it was up to the carriers  
16 to decide -- and instead issued a broad national  
17 noncoverage policy, in April of '97. However, prior  
18 to the implementation of this noncoverage policy, the  
19 American Physical Therapy Association, APTA, and five  
20 individual plaintiffs, filed suit in Federal District  
21 Court in Massachusetts, and the case is called Aitken  
22 v. Shalala, to challenge the national noncoverage  
23 determination.

24 What happened since then is the Court  
25 issued a preliminary injunction preventing HCFA from

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1 issuing the national noncoverage policy and instead

2 remanded the issue back to the Agency to either  
3 provide a more detailed explanation of the  
4 noncoverage determination or revision of that  
5 determination. Since then, the policy has remained a  
6 carrier discretion.

7 Subsequent to the Court's decision, we  
8 took several actions, and we actually asked for three  
9 responses, and you have three letters in your packet.  
10 You may wish to refer to them during the course of  
11 your deliberations.

12 First is a January 23rd, 1998 letter from  
13 ECRI to the Agency, and ECRI primarily addressed two  
14 issues relating to the Court's decision. The purpose  
15 of the letter was to respond to the Court's decision.  
16 The first issue, and it's broken down in the letter,  
17 focused on wording of minimal versus no therapy, and  
18 the second issue centered on the statement that there  
19 were no comparative studies of electrical stimulation  
20 versus conventional therapy.

21 The second letter you have is an October  
22 14th, 1998 memorandum from AHCPR center for practice  
23 and technology assessment. Basically, this letter  
24 was to comment on the ECRI letter, and this memo  
25 opined that the overall conclusions of the original

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1 ECRI report remained valid, and they also commented  
2 on the guidelines for the treatment of pressure  
3 ulcers and noted that the guidelines simply state  
4 that electrical stimulation could be considered as  
5 treatment for certain pressure ulcers unresponsive to  
6 conventional therapy.

7 The final letter you had is an April 1,  
8 1999 letter to the Agency from the American Physical  
9 Therapy Association, commenting on the ECRI letter  
10 about the court decision and then the AHCPR letter on  
11 the ECRI letter. There's representatives from the  
12 American Physical therapy Association here today that  
13 can comment on the letter.

14 Now since the assessment, we have been  
15 meeting with interested parties on this topic, we  
16 have conducted a literature search of articles since  
17 the ECRI report and its update in 1997. We have  
18 provided the extracted literature search as well as

19 the articles as part of your packet, and that's  
20 identified as Appendix A, articles reviewed since the  
21 ECRI report.

22 It's important to note that we set broad  
23 search parameters in order to find as much relevant  
24 evidence as possible regarding the appropriateness  
25 and effectiveness of electrical stimulation. And

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1 those searches yielded clinical trials, case series,  
2 a meta-analysis, literature reviews, and we also  
3 included some opinion pieces. We also included  
4 several nonpublished articles that the APTA submitted  
5 to us that they felt were important to review.

6 Internally, we felt some questions about  
7 the adequacy of the evidence remained, so we decided  
8 to refer the issue to the Medicare Coverage Advisory  
9 Committee and that's how we got here today. Thank  
10 you.

11 MS. CONRAD: Thank you, Dr. Whyte. At  
12 this point, let's take a 15-minute break. Report  
13 back here about 10:40 or so.

14 (Recess taken.)

15 MS. CONRAD: Let's try to get started with  
16 the public presentations. The first speaker is Neil  
17 Spielholz from the American Physical Therapy  
18 Association, who will be followed by Joseph  
19 McCulloch.

20 DR. SPIELHOLZ: Good morning. My name is  
21 Dr. Neil Spielholz. I am a physical therapist and  
22 professor of physical therapy at the University of  
23 Miami School of Medicine. I am here on behalf of the  
24 American Physical Therapy Association and its 65,000  
25 members. I have no current or past financial

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1 interest in any manufacturer whose products are under  
2 discussion today. I am requesting that my testimony  
3 today along with my written statement that was  
4 already distributed to the panel members, be included  
5 in the permanent record of this meeting.

6 The panel is being asked to address  
7 whether the evidence is adequate to draw conclusions  
8 about the effectiveness of electrical stimulation for  
9 the treatment of chronic ulcers. The APTA responds

10 unequivocally, yes. There is adequate evidence to  
11 support the use of electrical stimulation as an  
12 additional treatment to facilitate the healing  
13 process of recalcitrant wounds.

14 As you are aware, an assessment of the  
15 literature has been done. At the request of HCFA,  
16 ECRI completed a technology assessment of the use of  
17 electrical stimulation for the treatment of chronic  
18 wounds. In APTA's view, the technology assessment  
19 contains some serious flaws and consequently, APTA  
20 has concerns with the way this assessment presents  
21 the electrical stimulation studies and the results  
22 thereof.

23 APTA believes that with respect to the  
24 efficacy of electrical stimulation for chronic wounds  
25 compared to sham or placebo stimulation, this

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1 assessment contains inconsistencies and  
2 misrepresentations of those data and study methods.  
3 It is important to note that the ECRI report  
4 contained a number of positive conclusions concerning  
5 the effects of electrical stimulation on the healing  
6 of chronic wounds, but the report also questioned the  
7 value of a number of the underlying stimulation  
8 studies.

9 One specific is that the assessment  
10 mistakenly concluded that patients in the control  
11 groups of several studies received no treatment  
12 whatsoever for their wounds. Consequently, although  
13 ECRI specifically found that, quote, there was a  
14 significant difference in the normalized healing  
15 rates between some types of electrical stimulation  
16 and control groups, unquote, ECRI erroneously  
17 concluded that, quote, these studies only demonstrate  
18 that patients treated by electrical stimulation may  
19 heal faster than those undergoing no therapy at all,  
20 unquote.

21 This significant error resulted from a  
22 misinterpretation of the words sham or placebo in  
23 many of the underlying studies. In those studies,  
24 researchers gave patients in both the study group and  
25 the control group conventional therapy, which

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1 consists of moist dressings, wound cleaning,  
2 debridement, et cetera, if it was necessary. The  
3 patients in the study group also received electrical  
4 stimulation. Patients in the control group received  
5 in addition to conventional care, sham or placebo  
6 electrical stimulation, i.e., the units were not  
7 turned on. Unfortunately, ECRI interpreted the use  
8 of the words sham or placebo in these studies to mean  
9 that patients in the control group received no  
10 therapy at all. This is simply not correct.

11 As Judge O'Toole expressively concluded,  
12 quote, ECRI's statement that there are no studies  
13 which compare electrical stimulation to conventional  
14 treatment appears simply wrong, unquote. To verify  
15 and confirm this misunderstanding, APTA obtained  
16 affidavits from the primary investigators of several  
17 studies. These affidavits have been submitted to  
18 HCFA with our written testimony.

19 In at least three studies, not only was  
20 electrical stimulation plus conventional care  
21 compared to just conventional care, but a crossover  
22 design was also used. The technology assessment,  
23 however, fails to convey, except for one situation,  
24 that a number of patients in control groups who had  
25 made little or no improvement after a specified

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1 period of time, were allowed to cross over and have  
2 electrical stimulation added to their conventional  
3 care. When they did, the wounds healed.

4 This is evidenced in, if we could have the  
5 first overhead please, and unfortunately this is  
6 small and you can't see it, but from the study by  
7 Kloth and Feedar, as seen in Tables 1 and 2 of this  
8 article, nine of nine ulcers in the treatment group  
9 healed completely after an average of 7.3 weeks. By  
10 contrast, not only did none of the seven ulcers in  
11 the control group close after an average of 7.4  
12 weeks, some ulcers actually increased in size. And  
13 if I'm given a chance, I would like later to perhaps  
14 comment on what Dr. Turkelson said about this is  
15 possibly being a flawed outcome, but for now let me  
16 just continue with the results.

17 In fact as a group, talking about the

control group, the average change in ulcer size was an increase of almost 6.5 percent. Kloth and Feedar then described how three of these patients were then crossed over and had electrical stimulation added to their ongoing conventional care. Their average healing rate then increased and all wounds closed within 8 weeks. From this study then, we have actually 12 of 12 treated wounds that closed.

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There is also from the paper by Gentzkow et al., as seen from Figure 1 of this paper, during the first four weeks of the study, wounds in the treatment group had decreased in area an average of 49.8 percent. In the same time frame, ulcers in the sham treatment group increased an average of 23.4 percent. 15 patients out of these 19 in the sham group were then crossed over to receive electrical stimulation. The wounds in these patients had only closed an average of 13.4 percent during the four weeks of sham treatment. In other words, these 15 patients were a subgroup of the original group, which is why they had a somewhat lower heal rate. The wounds in these patients had only closed an average of 13.4 percent during the four weeks of sham treatment, but this then increased to a closure of 47.9 percent less than their size at time of crossover. In other words, there was a four-fold increase in healing during four weeks of stimulation, versus four weeks of sham treatment in the same ulcers.

In fact, at the end of an average of nine weeks, 40 percent of these ulcers were then healed completely. A similar percentage of ulcers, or 41 percent, had healed in the active treatment group

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over an average of 11.8 weeks.

In the paper by Baker et al., and again, don't do overheads on HF printers, it just smears too much, but basically what this is supposed to have shown is that 11 patients had wounds that were treated first under the control protocol and then later under one of two stimulation protocols. The mean healing rate for these patients during the

9 control protocol was 9.7 percent, and this increased  
10 to 43.4 percent per week during active treatment.  
11 Seven of these crossed over patients healed during  
12 the stimulation period.

13 It should also be noted that the  
14 recognition of what happened to the crossover  
15 patients in these and other studies invalidates other  
16 criticisms leveled by ECRI that imply that the  
17 control patients in all these studies were somehow  
18 and for some reason at a healing disadvantage  
19 compared to the patients who received treatment.  
20 ECRI failed to address the significance of these  
21 crossover findings.

22 On the basis of these and other concerns,  
23 APTA would like to caution the panel against  
24 formulating a negative recommendation based on the  
25 unfounded criticisms of studies found in the ECRI

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1 technology assessment. It is our belief that these  
2 aforementioned studies are profound and render  
3 impressive positive results.

4 And there is additional evidence in the  
5 literature that demonstrates the efficacy of this  
6 intervention. Next overhead please. For example,  
7 Stiller et al. Had closure of 50 percent of wounds, 9  
8 of 18, was achieved over an eight-week period, while  
9 none of the control group healed. In Walcott et al.,  
10 75 percent, 6 of 8 chronic wounds healed over an  
11 average of 7.9 weeks, while none of nine in the  
12 control group healed. And in the Wood et al.  
13 Article, 58 percent, or 25 of 43 treated wounds  
14 closed compared to 3 percent, or 1 out of 33 in the  
15 control groups.

16 Indeed, we want to bring your attention to  
17 the fact that despite the criticism that ECRI levels  
18 against studies, their report still found the quality  
19 of the studies evaluating electrical stimulation to  
20 be roughly equivalent to the quality of similar  
21 published studies in other wound healing therapies.

22 And because my time is almost up, let me  
23 jump ahead, if I may. Can I have the next overhead  
24 please? APTA believes based on our assessment of the  
25 literature and all the evidence which is presented in

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1 detail in our written testimony, that it is clear  
2 that the evidence is sufficient to support the use of  
3 electrical stimulation for chronic pressure ulcers,  
4 chronic venous ulcers and chronic arterial ulcers.

5 Additionally -- next overhead, and this is  
6 the final -- additionally, the panel is being asked  
7 to place the therapy in a category of effectiveness.  
8 APTA believes the intervention could be placed in  
9 category of effectiveness 2, which is more effective,  
10 the new intervention improves health outcomes by a  
11 significant margin as compared with established  
12 services. However, since this intervention is not  
13 new and since it has become the standard of care,  
14 albeit adjunctive care for ulcers that fail to heal,  
15 the intervention could just as accurately be  
16 considered breakthrough technology, which is  
17 category 1.

18 There is adequate clinical evidence to  
19 conclude that electrical stimulation for chronic  
20 wounds is effective. Because its efficacy is  
21 supported by valid and reliable evidence and because  
22 of a profound benefit it can provide to needy  
23 Medicare beneficiaries who suffer from chronic  
24 wounds, APTA urges you to recommend to HCFA that the  
25 Agency ultimately issue a national coverage policy.

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1 Thank you.

2 MS. CONRAD: Thank you, Dr. Spielholz.  
3 Joseph McCulloch, followed by Jennifer Dexter.

4 DR. McCULLOCH: Good morning. My name is  
5 Dr. Joseph McCulloch and I'm here today representing  
6 the American Academy of Wound Management. The AAWM  
7 is a multidisciplinary certification agency that  
8 represents over 1600 physicians, nurses, physical  
9 therapists, and other health care providers who have  
10 achieved board certification as wound care  
11 specialists. As wound care specialists, members of  
12 the Academy understand well the benefits to be gained  
13 from the electrical stimulation in patients with  
14 chronic wounds, including both pressure, venous  
15 insufficiency and arterial ulcers.

16 As a matter of formality, I have no

17 current or prior financial interest in any  
18 manufacturer whose products are under discussion here  
19 today. I would also like to request that today's  
20 testimony, along with my written testimony, be  
21 included in the record.

22 There are have been numerous pieces of  
23 literature that examined the effectiveness of E-stim,  
24 which have been presented to the panel, including  
25 over 60 citations regarding the use of E-stim, and

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1 they were asked to ask whether the evidence was  
2 adequate to draw conclusions about the effectiveness  
3 of electrical stimulation as an adjunctive therapy  
4 for chronic wounds. Consistently the studies  
5 conclude that electrical stimulation is an effective  
6 adjunctive therapy in the treatment of chronic  
7 wounds. This literature only presents a portion of  
8 the studies that exist showing electrical stimulation  
9 as a beneficial and effective treatment for the  
10 healing of chronic wounds.

11 Of the over 60 articles provided to the  
12 panel, 14 articles were published after 1996. My  
13 testimony will focus on this new literature. The  
14 literature review is broken down by wound type, as  
15 the panel is considering the effectiveness of  
16 electrical stimulation on chronic pressure ulcers,  
17 venous insufficiency ulcers, and ulcers due to  
18 arterial insufficiency.

19 Beginning first with pressure ulcers. In  
20 1999, Lisa Ovington revisited the AHCPR guidelines  
21 concerning surgical dressings and adjunctive  
22 therapies for pressure ulcers. On the basis of new  
23 literature available since the AHCPR guideline was  
24 published, Dr. Ovington concluded that the strength  
25 of evidence rating should be raised from a B to an A.

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1 And A rating, the highest rating possible, is the  
2 result of two or more randomized control trials on  
3 pressure ulcers in humans. Ovington came to this  
4 conclusion after reviewing literature published after  
5 1993. Her work clearly demonstrates that the  
6 literature strongly supports the use of electrical  
7 stimulation in the treatment of wounds.

8 In 1996, Baker and all randomly assigned  
9 patients to four groups, three receiving treatment  
10 with differing wave forms. The fourth group received  
11 sham stimulation. It is important to note that all  
12 groups continued to receive standard wound care.  
13 After 28 days, the percentage of patients in  
14 treatment groups who were fully healed was nearly  
15 double those in the control group. Control group  
16 patients failing to heal were then allowed to cross  
17 over into a treatment group. A statistically  
18 significant result in healing rates resulted from the  
19 crossover.

20 AAWM recognizes that not all literature is  
21 positive. Sheffitt et al. Published a literature  
22 review in Ostomy and Wound Management in February of  
23 this year. The review is rather limited and in fact  
24 some of the literature reviewed were not published  
25 studies. The authors did not conduct a critical

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1 review of the actual literature but merely reviewed  
2 the literature abstracts and then drew their  
3 conclusions. Moreover, the reviews by the authors  
4 are misrepresented and the article suggests research  
5 protocols that are clinically unreasonable,  
6 unrealistic, and even unethical. This article has  
7 come under serious criticisms by Dr. Spielholz, who  
8 you just heard from, and Luther Kloth, as being  
9 biased and misleading about the articles it includes.  
10 This critique was published in a subsequent edition  
11 of the Journal.

12 Looking next at venous insufficiency. In  
13 1996, Kenkre conducted a randomized double blind  
14 control clinical trial, which assessed the effects of  
15 electromagnetic therapy on chronic venous ulcers in  
16 19 patients. 68 percent experienced improvement in  
17 ulcer size, and four individuals, 21 percent, healed  
18 completely. The control group was confined to  
19 receive conventional care. The results showed that  
20 the patients in the treatment group reported  
21 increased mobility, decreased pain, and greater  
22 healing. This new study provides additional support  
23 for the use of E-stim as an effective intervention in  
24 the treatment of venous ulcers.

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1 Gilchrist, a study on electrical stimulation was  
2 applied to treat skin perfusion in 132 patients with  
3 diabetes. The study analyzed the possible mechanism  
4 of wound healing action and the role electrical  
5 stimulation potentially played in that mechanism.  
6 While not a wound healing study per se, it did  
7 support the use of E-stim in older patients, and  
8 found that electrical stimulation increased blood  
9 flow and decreased edema, two of the primary  
10 obstacles in healing of the diabetic foot.

11 Also in 1998, Peters published the results  
12 of his study on the effect of galvanic electrical  
13 stimulation on vascular perfusion in diabetic  
14 patients. In his study, 11 of the 19 subjects were  
15 diagnosed with impaired peripheral perfusion. The  
16 subjects were studied over a two-day period. In the  
17 group with impaired peripheral perfusion, a  
18 significant rise in tissue oxygenation as compared to  
19 the control measurements, was measured during the  
20 first five minutes of stimulation,  $P .04$ . For those  
21 patients without vascular disease, there was not a  
22 significant increase compared to the baseline,  $P$  of  
23  $.28$ . What Peters' data suggests is that external  
24 subsensory electrical stimulation induces a transient  
25 rise in skin perfusion in persons with diabetes and

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1 impaired peripheral perfusion. Such a development  
2 can be contributory to the promotion of healing.

3 In 1997, Jacques published a case report  
4 of an 81 year old male with several nonhealing stage  
5 IV ulcers on his right foot. The patient was  
6 hospitalized for five months with no improvement. He  
7 was then placed on high voltage electrical  
8 stimulation for 30 minutes five days a week, and  
9 obtained 100 percent closure of all ulcers within  
10 eight weeks. In their discussions the authors write,  
11 quote, the successful use of electrical stimulation  
12 in this case was impressive. The usual modalities in  
13 treating nonhealing ulcers had proven unsuccessful.  
14 There was consensus among medical and surgical  
15 consultants that amputation was the only alternative.

16 End quote.

17 The electrical stimulation of this patient  
18 was certainly breakthrough technology, since nothing  
19 else had worked and amputation was being considered,  
20 thus supporting the notion that electrical  
21 stimulation should be covered when conventional  
22 therapy fails.

23 In 1997, Baker et al. Published a  
24 randomized control trial of 80 diabetic patients with  
25 114 wounds, the duration which ranged from six to 640

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1 days. This study compared four groups, two receiving  
2 different types of electrical stimulation, and two  
3 very low level or no stimulation. All groups  
4 continued to receive standard wound management.  
5 Stimulation with A protocol, which was the asymmetric  
6 biphasic wave form, enhanced healing by 60 percent.  
7 Stimulation with the B protocol, which was symmetric  
8 biphasic, did not increase the healing rate when  
9 compared to the control groups.

10 In other and mixed categories, the 1997  
11 article by Frantz in Clinical Geriatric Medicine,  
12 reviews a number of adjunctive treatments for  
13 recalcitrant wounds, including electrical  
14 stimulation. After reviewing eight reports which  
15 studied 255 patients in total, the article concludes  
16 that although the individual sample sizes were small,  
17 quote, these studies suggest that application of  
18 electrical stimulation has the potential of enhancing  
19 the healing of chronic recalcitrant wounds, end  
20 quote. The paper goes on to mention a ninth study  
21 that used 185 ulcers, again with good results in the  
22 treatment groups. Thus in this review alone, there  
23 is an overall sample size of 430 ulcers.

24 Luther Kloth and I published an article in  
25 Advances in Wound Care in 1996, which summarized 13

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1 clinical studies showing accelerated healing of  
2 recalcitrant pressure ulcers, and 14 in vivo studies  
3 which investigated how various aspects of the healing  
4 process were positively influenced by electrical  
5 stimulation. The paper includes a summary of how  
6 electrical stimulation parameters can be varied



7 depending on the therapeutic goals desired.

8 In summary, because of the efficacy of  
9 electrical stimulation as supported by valid and  
10 reliable evidence and because of the profound benefit  
11 it can provide to needy Medicare beneficiaries who  
12 suffer from this condition, the AAWM urges you to  
13 reach a positive recommendation on the conclusion of  
14 your proceedings today. Thank you.

15 MS. CONRAD: Thank you, Dr. McCulloch.  
16 Jennifer Dexter, followed by Diane Krasner.

17 MS. BERNISSE: Good morning. My name is  
18 Katy Bernisse. I am here on behalf of Jennifer  
19 Dexter, and I am assistant vice president for  
20 government relations for the Easter Seals national  
21 headquarters. Easter Seals appreciates the  
22 opportunity to contribute to the advisory committee's  
23 evaluation of electrical stimulation in healing  
24 chronic wounds. Easter Seals believes that  
25 electrical stimulation is a useful and effective

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1 treatment in promoting the healing of chronic wounds  
2 to improve health, function and independence.

3 Easter Seals supports the findings and  
4 recommendations of the American Physical Therapy  
5 Association regarding this adjunctive therapy.

6 Easter Seals is a national nonprofit  
7 organization that is dedicated to helping people with  
8 disabilities achieve independence. For more than 80  
9 years, Easter Seals has provided home and community  
10 based services and advocacy for children and adults  
11 with disabilities. Each year Easter Seals serves  
12 more than one million people through a national  
13 affiliate network operating more than 400 service  
14 sites. Easter Seals provides medical rehabilitation  
15 and other services to tens of thousands of Medicare  
16 beneficiaries, including many with chronic and  
17 significant impairments. Easter Seals services are  
18 provided at home, comprehensive outpatient  
19 rehabilitation facility, rehabilitation agency,  
20 skilled nursing, and other settings.

21 Easter Seals therapists report that  
22 electrical stimulation is an effective intervention  
23 that contributes to the healing of most types of

24 wounds including pressure, venous stasis, diabetic,  
25 and neuropathetic ulcers, and ulcers due to arterial

00094

1 insufficiency. This treatment is an effective and  
2 important option in incidents where wound healing is  
3 not progressing.

4 Easter Seals uses a holistic approach to  
5 patient care, where electrical stimulation augments  
6 other wound care and patient education and training.  
7 Staff inform and assists clients and family members  
8 on skin care and healing, often addressing issues  
9 relating to incontinence, nutrition, transfer and  
10 mobility, prosthetic care, and environmental risks.

11 Let me share one example cited by an  
12 Easter Seals therapist in response to our inquiry  
13 concerning the effectiveness of this therapy. He  
14 reported that electric stimulation was particularly  
15 helpful in healing a chronic wound on the heel of a  
16 75 year old man. This man had preexisting upper and  
17 lower limb amputations and despite aggressive  
18 dressing changes and other care, the open wound on  
19 his heel simply would not heal. He risked bone  
20 infection and possible loss of his one remaining  
21 foot. Electrical stimulation facilitated healing and  
22 contributed to an overall improvement of this man's  
23 health, function, mobility and quality of life. We  
24 believe that this successful experience is  
25 representative of the benefits of this adjunctive

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1 treatment.

2 Easter Seals encourages the committee to  
3 consider our positive experience with using electric  
4 stimulation for healing chronic wounds. It is a  
5 valuable component of comprehensive wound treatment,  
6 which fosters improved health outcomes and associated  
7 benefits to beneficiaries and society. We believe  
8 that research findings support the effectiveness of  
9 electric stimulation as an adjunctive therapy for  
10 chronic ulcers. Easter Seals hopes the Advisory  
11 Committee will conclude likewise in its analysis of  
12 the issue.

13 My colleague, Rini Catalar, assistant vice  
14 president for medical health services for Easter

15 Seals and an experienced physical therapist, and  
16 other staff are available to answer questions and  
17 provide additional information to assist the  
18 committee in its analysis. Contact information is in  
19 our testimony. We appreciate the opportunity to  
20 share our views today. Thank you very much.

21 MS. CONRAD: Thank you. Diane Krasner,  
22 followed by Joseph Cavorsi.

23 DR. KRASNER: Good morning. I am  
24 Dr. Diane Krasner, and I am I here to read a  
25 statement on behalf of the National Pressure Ulcer

00096

1 Advisory Panel. I served on the panel from 1992 to  
2 1994 and am currently an alumni member.

3 The NPUAP is an independent not-for-profit  
4 organization dedicated to the prevention an  
5 management of pressure ulcers through education,  
6 research and public policy. Formed in 1987, the  
7 NPUAP is comprised of leading authorities  
8 representing various disciplines, including medicine,  
9 nursing, research, physical therapy, nutrition, and  
10 education. The NPUAP has a long history of  
11 collaborating with HCFA on a number of issues,  
12 including the PUSH tool for use on the MDS PAC,  
13 assisting with development of categories and usage  
14 guidelines for dressing and support surfaces, and  
15 assisting with the development of quality indicators  
16 for the MQIS pressure ulcer module.

17 The NPUAP supports the use of electrical  
18 stimulation as a generally acceptable method for  
19 pressure ulcer healing. Presently, physicians and  
20 physical therapists use E-stim as an adjunctive  
21 therapy for non-healing pressure ulcers. The U.S.  
22 AHCPR guidelines on the treatment of pressure ulcers,  
23 1994, recommends its use for both Stage III and Stage  
24 IV pressure ulcers that have proved unresponsive to  
25 conventional therapy. Moreover, the AHCPR has noted

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1 that E-stim can also be used successfully in  
2 recalcitrant Stage III pressure ulcers.

3 You heard Joe McCulloch previously discuss  
4 the update to the AHCPR recommendation that Lisa  
5 Ovington published in 1999 that proposes elevating

6 the strength of the evidence to an A rating, and you  
7 also heard previously cited Gardner and Frantz's 1999  
8 meta-analysis, which suggests strong evidence for the  
9 effectiveness of E-stim.

10 The NPUAP recognizes that HCFA has raised  
11 some concerns on the efficacy of E-stim based on the  
12 ECRI report. However, given the methodological  
13 issues raised in the analyses within the report,  
14 there were also many positive findings. Most  
15 notably, E-stim facilitates the healing of chronic  
16 wounds, pulsed current electrical stimulation  
17 provides the normalized healing rates of Stage II to  
18 Stage IV pressure ulcers, and alternating current  
19 E-stim improves the normalized healing rates of  
20 pressure ulcers.

21 The NPUAP agrees that more well designed  
22 clinical trials should be conducted. However,  
23 present studies do suggest that E-stim is effective  
24 in the healing of recalcitrant pressure ulcers as  
25 evidenced in the AHCPR pressure ulcer treatment

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1 guidelines. Until such trials are completed, HCFA  
2 can rely on the present studies and considerable  
3 expert opinion and experience which clearly suggests  
4 a positive difference in the use of E-stim in healing  
5 recalcitrant Stage II to Stage IV pressure ulcers.

6 And with your permission, Dr. Garber, I  
7 would like to either now or later, but since I have a  
8 few minutes, make a couple of comments on my own as  
9 an individual.

10 As some of you know, I have been involved  
11 in chronic wound healing for many years. I co-edit  
12 the major text in the area of chronic wound care, and  
13 I am the co-director of the interdisciplinary  
14 international wound care course at the University of  
15 Toronto. And I just, in listening to the comments  
16 this morning, wanted to speak to two points.

17 One is the problems with RCT as a gold  
18 standard for this patient population. They leave  
19 much to be desired because of the variability in this  
20 patient population in particular. It is estimated  
21 that only 20 percent of chronic wound patients meet  
22 the inclusion criteria in these studies, and so what

23 about the other 80 percent, the ones with all the  
24 co-morbidities and co-factors that drop out of these  
25 studies? The diabetics, the people with adherence

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1 problems. It just is an issue that we come against  
2 again and again as we evaluate dressings and new  
3 technologies, but it's a very real problem if we only  
4 really on RCTs.

5 And the second is the caution that if we  
6 only use time to healing as an outcome measure, I  
7 think we are doing a disservice. In fact, probably a  
8 more significant variable based on the work, the  
9 meta-analyses and the epidemiological work that  
10 Dr. Margolis is doing at Penn is how long the wound  
11 has been present in the first place. There are other  
12 significant outcome measures especially that should  
13 be considered for E-stim in future studies, and that  
14 includes reduction in pain in chronic wound patients  
15 and increasing their quality of life. Thank you.

16 MS. CONRAD: Thank you, Miss Krasner.  
17 Joseph Cavorsi, followed by Pamela Unger.

18 DR. CAVORSI: Good morning. My name is  
19 Dr. Joseph Cavorsi; that's Italian, not Cavorski, or  
20 Polish, and certainly not Kevorkian.

21 (Laughter.)

22 I am a board certified general and  
23 vascular surgeon by trade. I have been in practice  
24 since 1984. I am also the medical director of a  
25 multidisciplinary hospital based outpatient wound

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1 care center that treats nearly 1700 patient visits  
2 per month. I repeat, 1700 patient visits per month,  
3 dealing exclusively with the diagnosis and treatment  
4 of all forms of chronic nonhealing wounds.

5 For the record, I have no financial or  
6 other interest in any product which delivers the  
7 intervention that is the subject of today's hearing.

8 It is my understanding that the panel has  
9 been asked to determine whether the evidence, both  
10 clinical and scientific, is adequate to allow  
11 conclusions to be drawn regarding the effectiveness  
12 of electric stimulation in the treatment of chronic  
13 wounds. I wish to thank the panel for the

14 opportunity to express my opinion regarding this very  
15 important subject. I come to you not as a research  
16 scientist, a general quoting one study after another,  
17 I have no large database for you to review. I come  
18 to you as a physician who has extensive clinical  
19 experience dealing with real patients with real  
20 wounds on a daily basis.

21 My initial experience with electric  
22 stimulation was strictly incidental. In early 1992  
23 while making early rounds on a patient of mine with a  
24 pressure ulcer on her sacrum, I noted another patient  
25 in the adjacent bed with a similar sacral wound.

00101

1 Oddly, however, attached to a small apparatus with  
2 wires and an electrode. The young lady attending the  
3 machine, who turned out to be a physical therapy  
4 assistant, was kind enough to briefly describe the  
5 beneficial effects of electric stimulation in wound  
6 care when I questioned her. However, when asked for  
7 the scientific basis for her contention, she could  
8 not respond.

9 I shrugged the notion off. I watched the  
10 same therapist methodically set up her apparatus,  
11 with curiosity, on a daily basis. Both patients  
12 received excellent care. The pressure ulcers were  
13 properly off-loaded, they were free of nonviable  
14 necrotic tissue, and provided with protective  
15 moisture retentive occlusive dressings. Both  
16 patients were receiving nutritional support.  
17 However, my curiosity soon turned to amazement when I  
18 realized that the other patient's wound was healing  
19 better, developing healthier and more granulation  
20 tissue, and contracting or closing faster than mine  
21 was.

22 I was in turmoil. Was this just a  
23 coincidence? I spoke to the therapist's program  
24 director and requested any literature she had  
25 available regarding the use of electric stimulation

00102

1 in the treatment of wounds. She immediately provided  
2 me with nearly 40 articles, the majority of which  
3 were physical therapy based. I read each one, paid  
4 particular attention to any prospective randomized

5 controlled studies. Although there was much  
6 variation in how these studies were conducted, one  
7 common dominator was repeatedly evident. The study  
8 or treated group with electric stimulation fared  
9 significantly better than the placebo or control  
10 group.

11 I was still not convinced. I personally  
12 researched the literature and encountered excellent  
13 preclinical studies showing that externally applied  
14 electric stimulation can increase the synthesis of  
15 structural proteins, stimulate neoangiogenesis,  
16 facilitate the migration of epithelial and fibroblast  
17 into a wound site, cells that are essential in the  
18 normal healing process, reduce edema, inhibit the  
19 growth of infectious pathogens, and even accelerate  
20 the recovery of damaged nerve tissue. Certainly all  
21 positive effects when related to wound healing.

22 Soon after, I ordered electric stimulation  
23 for the first time in a patient of mine with a  
24 recalcitrant diabetic foot ulcer, who was not  
25 responding to the usual standard of care. He went on

00103  
1 to heal uneventfully. I was not convinced.

2 My early experience with electric  
3 stimulation and wound healing was used only in  
4 patients who failed to heal with the usual standards  
5 of care. For example, patients with ischemic ulcers  
6 that were not candidates for arterial reconstructive  
7 surgery. Patients with venous ulcers who failed  
8 conservative compression therapy. Diabetic patients,  
9 or patients with pressure ulcers who did not respond  
10 to proper off-loading, debriding and protection.  
11 Although all these wounds were caused by different  
12 etiologies, they all had one thing in common, their  
13 inability to heal, regardless of whether they were  
14 receiving appropriate care. They became chronic. No  
15 longer could they follow the orderly and predictable  
16 path to normal healing. It was my early experience  
17 that the addition of electrical stimulation in  
18 conjunction with good wound care reestablished that  
19 path to normal healing.

20 As my experience increased with the use of  
21 electric stimulation with chronic wounds, I began to

22 use this modality, not only in patients who failed  
23 the usual standards of care, but as an adjunct in all  
24 patients with chronic wounds. I soon realized that  
25 these patients healed faster than the patients who

00104

1 were treated with standard care alone without  
2 electric stimulation. This fact turned out to be  
3 extremely important, especially to my diabetic  
4 patients who are at the greatest risk for infection  
5 the longer that wound remains open, thus exposing  
6 them to possible limb loss or even death.

7 Obviously, wounds healing faster is  
8 naturally more cost effective. We have entered the  
9 21st century. We will have other wound care issues  
10 to deal with in the future. I predict wound care  
11 will become a medical specialty in and of itself. We  
12 no longer treat chronic wounds passively with just  
13 wound dressings, hope and pray that the body will  
14 heal itself when it does not have the ability to do  
15 so. Today we have the opportunity to treat chronic  
16 wounds more proactively.

17 Electric stimulation has proven effective  
18 in that ultimate goal both in the experience of this  
19 of this clinician and as evidenced in the volume of  
20 literature that now exists. I implore this panel to  
21 give this subject their sincerest consideration, as  
22 I'm confident you will. To abandon this capability  
23 now, especially after so much success over the last  
24 eight years, not to provide this truly revolutionary  
25 method of assisting wound healing to a segment of our

00105

1 population who need it the most, the Medicare  
2 patient, would be a travesty. The use of electric  
3 stimulation as an adjunct treatment in the care of  
4 chronic wounds has become the standard of care in my  
5 community. Please, do not send my practice protocols  
6 back to the dark ages. Thank you for your attention.

7 MS. CONRAD: Thank you, Dr. Cavorsi.  
8 Pamela Unger, followed by Luther Kloth.

9 MS. UNGER: Good morning. I am Pam Unger,  
10 a physical therapist, and also a certified wound care  
11 specialist. I today am representing the Association  
12 for the Advancement of Wound Care, of which I am a



13 current board member. The association is an  
14 interdisciplinary organization that has over 950  
15 members. Those members include nurses, physicians,  
16 podiatrists, physical and occupational therapists,  
17 and industry members. The association and  
18 organization gives its members the opportunity to  
19 build a collaborative community to facilitate optimal  
20 wound care for millions of people who suffer with  
21 chronic wounds. Our members have and do currently  
22 provide electrical stimulation on patients with  
23 chronic wounds. We have seen first hand through  
24 clinical intervention the effectiveness electrical  
25 stimulation has on chronic wound healing.

00106

1 I have personally used electrical  
2 stimulation as an adjunctive therapy in my clinics  
3 and practices since 1980. In my own clinic,  
4 electrical stimulation is now a standard of care. I  
5 have no current or past financial interest in any  
6 manufacturer whose products are under discussion  
7 today. I am requesting that my testimony be  
8 submitted, along with the written statement that has  
9 already been distributed to the panel member, and  
10 included in the permanent record of the meeting.

11 On behalf of the Association for the  
12 Advancement of Wound Care, the evidence does  
13 overwhelmingly support the effectiveness of  
14 electrical stimulation in the treatment of wounds.  
15 The AAWC, which is our abbreviation for the  
16 association, would like to present the panel case  
17 studies that show clinical evidence. As such, the  
18 AAWC would like to focus our testimony on the  
19 clinical applications and effectiveness of electrical  
20 stimulation in the treatment of chronic wounds.

21 Before I embark on showing you some slides  
22 and case studies, I would also like to ask the panel  
23 what a wound really is and when a wound becomes  
24 chronic. A wound is an injury to the skin, which I'm  
25 sure all of you are well aware of. The skin happens

00107

1 to be the largest organ in our body and in fact, I  
2 would think that the healing process, regardless of  
3 what the underlying etiologies or comorbidities may

4 be, would be the same, certainly knowing that those  
5 variables could in some way, shape or form slow that  
6 healing process or alter the rate of healing.

7 Because there's been such a large amount  
8 of literature that has been in front of you related  
9 to pressure ulcers, I will not show you a pressure  
10 ulcer case study. We will talk about those other  
11 types of wounds that have been extremely, benefitted  
12 extremely from the use of electrical stimulation. So  
13 if we can -- and we need to turn the lights down, I'm  
14 certain, so that we can see.

15 This first patient happens to be the case  
16 study that I think you have in front of you noted as  
17 DL, happens to be a 47 year male. Now some may say  
18 well, gee, that's not our Medicare population. This  
19 happens to be a disabled gentleman who has been on  
20 Medicare benefits since one year prior to us noting  
21 this wound. He was evaluated in March of 1996 in our  
22 clinic. He has ulceration on his left B/K amputation  
23 site, the amputation had been two years prior. The  
24 patient actually has a past medical history that  
25 includes ministroke and Beurger's disease, which is

00108  
1 in fact the most significant thing as to why the  
2 ulcer occurred.

3 His treatment prior to coming to our  
4 clinic was silvadene and a dry sterile dressing. We  
5 actually looked at this patient looking at an onset  
6 of nearly six to eight months prior to him seeing us,  
7 that what he may need is some debridement, which  
8 would have to be approached in a very cautious  
9 fashion, electrical stimulation, and our  
10 recommendation for dressing was a saline gauze with  
11 an occlusive dressing, to obtain some autolytic  
12 debridement. He was also not allowed to wear his  
13 prosthesis, so that there would not be any increased  
14 pressure on that area.

15 The goal of course for this patient was to  
16 avoid revision of the amputation; that was what was  
17 recommended by two previous surgeons who saw the  
18 patient. Patient also had two vascular evaluations.  
19 Numerous arteriograms were done to find that there  
20 was absolutely no possibility of revascularizing this

21 patient.

22 Hence, we embarked on a program of  
23 electrical stimulation. The patient's goal was to  
24 return to work. He certainly wanted to be able to  
25 ride his motorcycle, which was at the top of his

00109

1 list, probably even rated above returning to work.

2 As you can see, in two months time there  
3 was a significant reduction in the necrotic tissue.  
4 There we have what's looking to be a granulating  
5 wound bed, certainly some reddened area around the  
6 wound periphery.

7 At approximately six months after treating  
8 this patient, we are at a nearly healed position, at  
9 which point by certainly nine months, which you may  
10 think is a rather long period of time, nothing was  
11 working with the patient previously, the wound was  
12 completely healed. He has not ever since that point  
13 in time had this wound revised, or had the amputation  
14 revised; he still in fact is a B/K amputee. His  
15 alternative was an A/K amputation or may have  
16 actually been a hip disartic, which would have  
17 certainly limited his ability to return to the work  
18 force. The patient could in fact return to the work  
19 force, get off of his Medicare disability, and  
20 certainly improve his quality of life.

21 Our next patient is an arterially  
22 insufficient patient. This will be listed as case  
23 study WM on your information that was given to you  
24 recently. He is a 66 year old white male. We  
25 evaluated him the end of March. He was actually

00110

1 admitted to the hospital for an amputation or  
2 possible revascularization. The patient had actually  
3 been treated for eight weeks prior at home. His  
4 treatment was to have a Betadine with dry sterile  
5 dressing. The patient has a past medical history  
6 which includes PVD, insulin dependent diabetes,  
7 hypertension, and he has had previous arterial bypass  
8 surgery.

9 When he was hospitalized, an anciebracheal  
10 index was obtained on the patient and his ABI was  
11 0.43. The patient rated his pain at 19 over 10,

12 essentially off the pain scale. He was very very  
13 uncomfortable and quite miserable as a patient. The  
14 other thing that complicated this is his wife, with  
15 whom he resided, indicated that she could not care  
16 for him at home and he needed to be admitted to a  
17 skilled nursing facility. The patient did not want  
18 his leg amputated and begged that in the clinic we  
19 would actually treat him with electrical stimulation  
20 and attempt to promote healing of this wound. That  
21 was a very dramatic type of intervention with this  
22 patient because there was so much pain associated  
23 with it.

24 What we did find was, though, not only  
25 could we get the wound to respond to the electrical

00111

1 stimulation, we could decrease the patient's pain.  
2 Certainly he had been medicated as well for pain  
3 control. We saw the patient on an outpatient basis  
4 three times a week. Of course our goal was to clean  
5 that up and maybe even have a potential of placing a  
6 skin graft on that if at all possible, to close it  
7 quickly.

8 On treating him with electrical  
9 stimulation, we actually noted in two months time,  
10 less than eight weeks, it was actually six weeks, the  
11 patient had a wound bed that was looking to have  
12 necrotic tissue sloughing. The patient did not  
13 receive any sharp debridement, of having the risk of  
14 having the patient undergo further amputation. It  
15 was all done with the use of an occlusive dressing  
16 and electrical stimulation. Now here is the patient  
17 actually four weeks post that, and we have a healed  
18 wound; a rather deformed scar, but a healed wound.  
19 Quite frankly, this patient salvaged his limb,  
20 salvaged his quality of life, and was allowed to  
21 continue to live at home with his family, which is  
22 certainly what his objective was.

23 The next patient case study I would like  
24 to present to you is a 65 year old female noted in  
25 your notes as DAL. This patient actually had an

00112

1 underlying diagnosis of venous insufficiency. She  
2 also has diabetes, and what she developed here on the

3 lateral portion of her leg is a vasculitic type of  
4 ulcer. Basically, this patient has had these ulcers  
5 for six months, has had severe pain associated with  
6 them, and she has gone from silvadene to Bacitracin  
7 to Neosporin, all with a dry sterile dressing on top  
8 of them. She actually was hospitalized because she  
9 was scheduled for bilateral amputations. The patient  
10 was not moving, was having multiple problems with her  
11 -- she had pneumonia a number of times, she had  
12 problems with asthma.

13 And she was evaluated by our clinic, at  
14 which time we recommended that we might be able to do  
15 some autolytic debridement to this, and follow this  
16 treatment with some electrical stimulation.  
17 Basically, we did use some hydrotherapy for about two  
18 days, to soften the tissue, but the pain was too  
19 great, so we stuck to the electrical stimulation.  
20 And because she was venous insufficient and had  
21 edema, we also used some light compression.

22 The patient in about three weeks time  
23 doesn't look tremendously better, although we were  
24 getting some autolytic debridement. Certainly by the  
25 time we're looking at eight weeks, we have a very

00113

1 nice looking granulating wound bed, and when we then  
2 went on to see the patient, from there we have all  
3 but a very small area, a two-centimeter area that was  
4 not healed. At this point the patient was fitted  
5 with a compression garment.

6 And then we have our patients always  
7 return to us in 60 days to insure that we've used as  
8 a maintenance prevention program works. This was the  
9 patient coming back to us in December. Very limited  
10 scar noted, and certainly a completely healed wound  
11 that has stayed healed.

12 I have one more patient case study which I  
13 can present to you, which is a neuropathic diabetic  
14 ulcer. This patient is 72 years old, believe it or  
15 not, owns a lighting company and works constantly,  
16 about ten hours a day. Unfortunately because of  
17 that, he did not have appropriate pressure relief.  
18 The patient had increased drainage, this wound had  
19 been present for approximately six months prior to

20 him seeing us. He needed debridement, and we  
21 utilized electrical stimulation along with a total  
22 contact cast. Basically the patient healed very  
23 dramatically in an eight-week period of time.

24 And I need to go on to say to you in  
25 conclusion that I certainly believe it is evident

00114

1 from the examples displayed that electrical  
2 stimulation for the treatment of chronic wounds is an  
3 effective and invaluable method of adjunctive  
4 therapy. The members of the AAWC treat a tremendous  
5 number of patients with chronic wounds. Our focus is  
6 to be a patient advocate. Patients will benefit from  
7 electrical stim as an adjunctive treatment, and it  
8 will assist with limb salvage and significantly  
9 improve the patient's quality of life.

10 Therefore, I respectfully request you as  
11 the panel to answer the question, is the clinical  
12 evidence supportive of the use of electrical  
13 stimulation for the treatment of chronic wounds yes.  
14 I would also recommend this adjunctive treatment for  
15 the treatment of chronic wounds be considered a  
16 breakthrough technology. I certainly implore you to  
17 recommend to HCFA for a national coverage policy for  
18 the use of electrical stimulation in the treatment of  
19 wounds.

20 MS. CONRAD: Thank you, Miss Unger.  
21 Luther Kloth, and next is Jerome Connolly.

22 MR. KLOTH: Good morning. My name is  
23 Luther Kloth. I'm a physical therapist, certified  
24 wound specialist, and fellow to the American Academy  
25 of Wound Management, also a professor of physical

00115

1 therapy at Marquette University, Milwaukee. I also  
2 practice at the wound clinic of a large hospital in  
3 Milwaukee. For the record, I have no financial  
4 interests in any product or device that delivers  
5 electrical stimulation to promote wound healing.

6 I speak to you today representing the  
7 National Consortium for Spinal Cord Medicine. This  
8 interdisciplinary consortium has recently published  
9 an evidence based clinical practice guideline in  
10 pressure ulcer prevention and treatment following

11 spinal cord injury. I hold up the guideline here for  
12 your observation.

13 This practice guideline represents the  
14 efforts of 19 professional health care member  
15 organizations. As stated in our request to speak  
16 today, the consortium has an interest in electrical  
17 stimulation to the extent that the guideline  
18 recommends the use of this modality in conjunction  
19 with standard wound care interventions for the  
20 treatment of Stage III and IV pressure ulcers.

21 Given that many if not most of these  
22 individuals who sustain spinal cord injuries are  
23 eligible for Social Security disability, and  
24 therefore may be Medicare beneficiaries, the  
25 consortium wishes to share its views with the panel

00116  
1 today. The 32 recommendations contained in the  
2 guideline represent, are based on an extensive review  
3 and analysis of the available scientific literature  
4 related to pressure ulcers.

5 Between the years 1966 and 1998,  
6 approximately 1800 abstracts were reviewed for  
7 relevance to the pressure and treatment of pressure  
8 ulcers. Nearly 350 articles were deemed relevant to  
9 the guideline and were retrieved. Of these, more  
10 than 200 clearly met the inclusion and exclusion  
11 criteria and were used for data extraction. Panel  
12 members were assigned relevant articles with evidence  
13 tables for study and consideration. From all of the  
14 evidence presented in the guideline, a methodology  
15 team used the hierarchy of scientific evidence  
16 described by Sackett, that employs five levels of  
17 scientific evidence as follows, and you see those  
18 five levels of scientific evidence posted on the  
19 screen.

20 A Level I scientific evidence was assigned  
21 for large randomized trials with clearcut results,  
22 Level II, Level III, Level IV and Level V, Level V  
23 being the lowest of the case studies and no controls.  
24 In addition, each study was evaluated for internal  
25 and external validity. Each recommendation was then

00117  
1 classified depending on the level of scientific

evidence supporting this specific recommendation. Categories and the strength of evidence associated with the recommendations are as follows, as shown on this overhead.

An A strength of evidence was assigned if the guideline recommendation was supported by one or more Level I study; B strength of evidence was assigned if the guideline recommendation was supported by one or more Level II studies; and a C recommendation was assigned if the guideline recommendation was supported only by Level, III, IV and V studies. Scientific evidence supporting electrical stimulation came from Levels I and II, which yielded a grade recommendation of A.

After discussion of each recommended guideline and the supporting evidence, the level of panel agreement with the guideline recommendation was assessed as either low, moderate or strong. In this assessment, each of the 19 panel members was asked to indicate his or her level of agreement on a five-point scale, with one corresponding to neutrality and five representing maximum agreement. The levels of panel agreement with the recommendation are shown on the screen, with low support within the

range of 1.0 to 2.32; moderate, 2.33 to 3.66; and strong, 3.67 to 5.0. For electrical stimulation, the strength of panel opinion was strong.

The strength of evidence came from three randomized control trials involving a total of 251 spinal cord injured individuals, each with at least one pressure ulcer that had not responded to treatment with standard wound care. Having completed the foregoing very thorough process, the multidisciplinary Consortium for Spinal Cord Medicine recommends the use of electrical stimulation in conjunction with standard wound care interventions for the treatment of Stage III and IV pressure ulcers.

In addition to the clinical practice guideline issued by the consortium, the Agency for Health Care Research and Quality, formerly the Agency for Health Care Policy and Research, published the



19 clinical practice guideline on the treatment of  
20 pressure ulcers. AHCPR was and is the lead  
21 government agency charged with supporting research  
22 designed to improve the quality of health care,  
23 reduce its costs, and broaden access to essential  
24 services. The practice guideline established an  
25 algorithm for the evaluation and management of

00119

1 pressure ulcers. The guideline concluded that  
2 electrical stimulation is the only adjunctive therapy  
3 with sufficient supporting evidence to warrant  
4 recommendation by the panel.

5 AHCPR recommended that a physician should  
6 consider a course of treatment with electrical  
7 stimulation for Stage III and IV pressure ulcers, and  
8 recalcitrant Stage II ulcers. More specifically, the  
9 AHCPR guideline noted, quote, data from five clinical  
10 trials involving a total of 147 patients support the  
11 effectiveness of electrical therapy in enhancing the  
12 healing rate of pressure ulcers that have been  
13 unresponsive to conventional therapy, end quote.  
14 This finding was consistent across the variety of  
15 electrical stimulation protocols.

16 The AHCPR guideline offers a comprehensive  
17 program for treating adults with pressure ulcers and  
18 included recommendations for ulcer care based on an  
19 expert panel's review of the accumulated scientific  
20 evidence as well as the collective clinical expertise  
21 of the panel members. Recommendations were assigned  
22 a strength of evidence rating of A, B or C, according  
23 to the following criteria shown on the screen.

24 An A rating would result from two or more  
25 RCTs on pressure ulcers in humans. B, results of two

00120

1 or more control clinical trials on pressure ulcers in  
2 humans, or when appropriate, results of two or more  
3 control trials on an animal model. And C, results of  
4 a single control trial or at least two cases series  
5 or descriptive studies on pressure ulcers in humans,  
6 or expert opinion. In 1994, the AHCPR guideline  
7 reflected the knowledge at the time of publication.  
8 At that time the strength of evidence rating was B.  
9 As recognized by the panel members, the assignment of

10 a B rating to electrical stimulation for wounds was a  
11 conservative one. Many panel members believed there  
12 was sufficient evidence to justify an A rating.

13 However, since there were multiple  
14 modalities included in the electrical stimulation  
15 studies reviewed, the study sample sizes were  
16 relatively small, and the therapy had not at that  
17 time been widely incorporated into practice. As  
18 such, the panel took a more conservative position in  
19 assigning strength of evidence to its recommendation.

20 As of May 1998, the AHCPR recommendation  
21 was five years old. Dr. Lisa Ovington reevaluated  
22 the AHCPR rating based on current evidence and the  
23 fact that electrical stimulation is now widely  
24 incorporated into clinical practice. Dr. Ovington  
25 found that based on all the evidence including

00121  
1 studies published subsequent to the review for the  
2 1994 guideline, the strength of evidence increased to  
3 an A rating. Dr. Ovington's review was published in  
4 volume 445 of Ostomy Wound Management in 1999.

5 As a result of its review of the  
6 literature and the development of the clinical  
7 practice guideline, the Consortium for Spinal Cord  
8 Medicine recommends the, and I quote, use of  
9 electrical stimulation to promote closure of Stage  
10 III and IV pressure ulcers, combined with standard  
11 wound care interventions, end quote. Moreover, based  
12 on its literature review, and the literature review  
13 conducted by AHCPR, as subsequently updated by  
14 Ovington, the Consortium for Spinal Cord Medicine  
15 concludes that the evidence is adequate to prove that  
16 electrical evidence is an effective treatment for  
17 patients with chronic pressure ulcers. The  
18 consortium places the intervention in a category of  
19 effectiveness of 2, more effective.

20 The consortium also feels that these  
21 results are applicable to the Medicare population,  
22 given that many if not most of these individuals are  
23 collecting Social Security disability and therefore  
24 will become Medicare beneficiaries, and the  
25 consortium urges the panel to conclude likewise.

00122

1 Thank you very much.

2 MS. CONRAD: Thank you, Mr. Kloth. Jerome  
3 Connolly.

4 MR. CONNOLLY: Thank you, Connie. Dr.  
5 Garber, members of the panel, my name is Jerome  
6 Connolly. I am a physical therapist. I am currently  
7 serving as the senior vice president for health  
8 policy of the American Physical Therapy Association.  
9 I have no current or past financial interest in any  
10 manufacturer whose products are under discussion  
11 today.

12 I speak to you today on behalf of the  
13 National Coalition for Wound Care. The National  
14 Coalition for Wound Care, of which APTA is a member,  
15 is a broad based coalition of ten member  
16 organizations representing over 100,000 providers,  
17 suppliers, manufacturers and clinicians with interest  
18 in the area of wound care. It is the mission of the  
19 NCWC to provide a forum for discussion among these  
20 groups and whenever possible, to provide a consensus  
21 opinion on issues in which the member groups have an  
22 interest. It is the consensus opinion of the NCWC  
23 that electrical stimulation has been proven to be an  
24 effective treatment for patients with all types of  
25 wounds, including venous stasis ulcers, pressure

00123  
1 ulcers, and ulcers due to arterial insufficiency.

2 This panel in its deliberations is  
3 contributing to a process undertaken by HCFA which is  
4 designed to attempt to develop Medicare coverage  
5 policy on the basis of evidence, employing evidence  
6 based medicine. Given this charge, it may be helpful  
7 to reflect for just a moment on the definition of  
8 evidence based medicine. According to Sackett, who  
9 is known in some circles to be called the father of  
10 evidence based medicine, EBM means, and I quote,  
11 integrating clinical expertise with the best  
12 available external clinical evidence from systematic  
13 research. EBM builds on and reinforces, but never  
14 replaces clinical skills, clinical judgment and  
15 clinical experience. End of quote. The coalition  
16 was pleased to note that the instructions to the  
17 panel today explicitly include direction to consider

18 clinical consensus information and clinical expert  
19 witness testimony in arriving at your conclusions.

20 We have heard today references to and  
21 discussion of an abundance of scientific and clinical  
22 evidence. It includes over 60 pieces of literature  
23 published in refereed journals, over 20 pieces of  
24 which have been published in the last four years. It  
25 includes a compelling presentation on the clinical

00124

1 application and the profound clinical effects of this  
2 adjunctive therapy. It includes presentations on  
3 clinical practice guidelines, including AAHCPR, which  
4 is a sister agency of HCFA under HHS, which concluded  
5 in 1994 in its guideline that, quote, electrical  
6 stimulation is the only adjunctive therapy with  
7 sufficient supporting evidence to warrant  
8 recommendation by the panel, end of quote. This  
9 recommendation, as we've heard, was based on a  
10 strength of evidence rating of B, the second highest  
11 rating possible, but four years later Ovington  
12 reviewed all the evidence including more recent  
13 literature, and concluding that strength of evidence  
14 should be increased to a strength of evidence of A,  
15 the highest possible rating.

16 Today's discussion also then included a  
17 consortium of spinal medicine, spinal cord medicine,  
18 and its clinical practice guideline, which represents  
19 the efforts of 19 professional health care member  
20 organizations. Over 350 articles were reviewed, and  
21 the strength of evidence rating again, received the  
22 highest possible rating, this time using a widely  
23 accepted methodology described by Sackett. The  
24 multidisciplinary consortium process resulted in a  
25 recommendation for the use of electrical stimulation

00125

1 in conjunction with standard wound care interventions  
2 for the treatment of Stage III and Stage IV pressure  
3 ulcers.

4 It was also acknowledged today that a  
5 technology assessment was conducted in 1996, and it  
6 did find fault in some of the studies it reviewed up  
7 to that time. Nevertheless, the assessment concluded  
8 that all studies reviewed, quote, had at least one

9 weakness but not all reported results were  
10 potentially confounded by these weaknesses, end of  
11 quote. In fact, that assessment concluded that  
12 electrical stimulation facilitates the healing rate  
13 of chronic ulcers, that it facilitates the complete  
14 healing of chronic ulcers, that pulsed current  
15 improves the normalized healing rate of Stage II  
16 through IV decubitus ulcers, that alternating current  
17 improves the normalized healing rate of decubitus  
18 ulcers, that devices used utilizing pulsed  
19 electromagnetic field improve the normalized healing  
20 rate of venous ulcers.

21 The ECRI report finally concluded that the  
22 quality of studies evaluating electrical stimulation  
23 is roughly equivalent to the quality of similarly  
24 published studies of other wound healing therapies.  
25 So one can conclude that the quality of the

00126

1 literature under discussion today was then about as  
2 good as it gets, and that given the abundance of  
3 literature published since the technology assessment  
4 that the evidence in support of electrical  
5 stimulation in the treatment of chronic wounds has  
6 only gotten progressively stronger.

7 Now it's always possible to find fault  
8 with the quality of studies, particularly when the  
9 research involves human subject design and in this  
10 case it involves multiple wound types and several  
11 different types of electrical stimulation. But in  
12 this case it almost approaches quibbling, given the  
13 abundance of the literature, the clinical case  
14 studies that you have seen, the expert witness  
15 testimony, and the considerable professional  
16 community consensus that is represented before you  
17 today by numerous multidisciplinary coalitions  
18 representing a broad cross-section of providers and  
19 practitioners.

20 One very compelling piece of literature  
21 that adds to if not sums up the discussion of this  
22 intervention and its effectiveness in the treatment  
23 of wounds is the meta-analysis conducted by Gardner  
24 and Frantz, that concludes that the rate of healing  
25 for stimulated wounds was more than double that of

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1       wounds just receiving conventional care.

2               It is clear then that the evidence is  
3       adequate, as is demonstrated by the literature, by  
4       the clinical case studies, by the consensus opinions  
5       of numerous experts, as well as several broad based  
6       coalitions of providers and practitioners. In the  
7       words of Judge George O'Toole, quote, the Agency must  
8       be careful not to transform an understandable  
9       preference for one kind of evidence into an  
10      impassible barrier, end of quote.

11              It's the position of the National  
12      Coalition for Wound Care that the evidence is  
13      adequate to enable conclusions to be drawn about the  
14      effectiveness of electrical stim in the treatment of  
15      chronic venous stasis ulcers, chronic wounds due to  
16      arterial insufficiency, and chronic pressure ulcers.  
17      The only remaining question then is, in what category  
18      of effectiveness should this intervention be placed?  
19      The categories of evidence as defined by HCFA before  
20      you, appear designed, at least in some cases, for new  
21      technology, which electrical stimulation is not. It  
22      is already being widely used based on its proven  
23      effectiveness. Thus, you might find that these  
24      definitions of categories for this particular  
25      instance, may need some refinement.

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1              The National Coalition for Wound Care  
2      believes the intervention could be placed in category  
3      2, more effective, and that reads, the new  
4      intervention improves health outcomes by a  
5      significant margin as compared with established  
6      services. However, since E-stim is not new, and  
7      since we have found and heard that it has become and  
8      it is the standard of care, albeit adjunctive care,  
9      for ulcers that fail to heal, the intervention could  
10     just as accurately be considered breakthrough  
11     technology, and in some instances in the clinical  
12     presentation, we found where it was in fact  
13     breakthrough technology, and in accordance with the  
14     definition of that category of effectiveness, it is  
15     the improvement in health outcomes is so large that  
16     the intervention becomes standard of care.

17 In summary, there is adequate evidence to  
18 conclude that electrical stimulation for chronic  
19 wounds is effective, and because its efficacy is  
20 supported by the valid reliable evidence and because  
21 of the profound benefit that it can provide to needy  
22 Medicare beneficiaries who suffer from this  
23 conditions, the National Coalition for Wound Care  
24 urges you to recommend to HCFA that the Agency  
25 ultimately issue a national coverage determination.

00129

1 Thank you.

2 MS. CONRAD: Thank you, Mr. Kloth.

3 This concludes the scheduled  
4 presentations. We're going to break for lunch. The  
5 panelists have asked that we have a working lunch.  
6 They are going to go get their lunch, bring it back,  
7 and eat here, and start their deliberations.

8 If anyone in the room wishes to address  
9 the panel again or anew, would you please let me  
10 know, and I will break out some time this afternoon  
11 for a panel presentation. You may use the aisle  
12 mikes, but please let me know. If I don't hear from  
13 you, I'm going to assume that you are all happy, and  
14 we will just continue.

15 DR. GARBER: Let me just add that I hope  
16 that all of the public speakers will be available. I  
17 suspect that the panel members will have questions  
18 for you. Thank you very much for the excellent  
19 presentations. We do hope that we can ask more of  
20 you to aid in our further deliberations.

21 MS. CONRAD: Okay. Let's meet back here  
22 at about 12:30.

23 (Luncheon recess.)

24 MS. CONRAD: Let's reconvene here. I have  
25 some public speaking requests. Each speaker will be

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1 allowed five minutes, beginning with Luther Kloth.

2 MR. KLOTH: Thank you. This morning after  
3 Dr. Frantz gave her presentation, which I felt was a  
4 very good presentation, I felt that based on some of  
5 the questions asked by the panel that perhaps there  
6 was clarification needed on the types of current,  
7 wave forms and so forth, so I wanted to do that.

8 First of all, the types of current that  
9 are available depends on whether you're talking to a  
10 physicist, sister or an electrical engineer, or a  
11 clinician who uses current to stimulate wounds, there  
12 will usually be two types of current, alternating  
13 current and direct current. The illustration which  
14 you saw this morning in Dr. Frantz's presentation was  
15 a unidirectional type of current, okay? The other  
16 type of current that is described and used in  
17 clinical use that biomedical engineers describe,  
18 clinicians describe, is called pulse current.

19 So we have AC, sinusoidal, DC and PC,  
20 okay? Now, in terms of clinical delivery of the  
21 currents, there are two methods of delivering current  
22 to the body. The clinical method that is used to  
23 deliver currents into wounds primarily from the  
24 studies, is called the method of capacity coupling.  
25 What that means is that you use two electrodes that

00131  
1 are in contact with the body. One electrode is in  
2 contact with the periwound skin, the intact skin  
3 surrounding the wound, the other electrode is applied  
4 directly to the wound tissue. Usually the current is  
5 conducted through some conductive medium such as  
6 saline, moist gauze, or some form of conductive  
7 material that's placed in the wound cavity with the  
8 electrode on top of that. That is called capacitive  
9 coupling and of course since you have two electrodes,  
10 you can assign a polarity, either positive or  
11 negative, to each of those electrodes.

12 The second method for introducing current,  
13 and we're talking about delivering current into the  
14 tissue, okay, with capacitive coupling, which is the  
15 most widely used method for electrical stimulation in  
16 wound healing. The other technique that, I think  
17 there were three or four studies, and one of those is  
18 the Salzberg study that was described earlier. That  
19 method uses a noncontact method called inductive  
20 coupling. It uses electromagnetic fields, pulsed  
21 electromagnetic fields, PEMF, okay, which is kind of  
22 akin to the devices that we use for bone healing.

23 So in that method you don't have an  
24 electrode, or electrodes attached to the tissue. You



25 have a device that is emitting the electromagnetic  
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1 field that then delivers that electromagnetic field  
2 into the tissues and once in the tissues, that  
3 electromagnetic field is converted to a current. So  
4 you're still delivering a current into the tissue in  
5 both cases, so I wanted to clarify that.

6 With regard to the common types of current  
7 that are used or described in the studies for  
8 electrical stimulation for wound healing, one type of  
9 current that is shown on this illustration is called  
10 high voltage pulse current. Why is it called high  
11 voltage? It's called high voltage because the  
12 duration of the baseline duration of each of those  
13 pulses that you see there is extremely short, about  
14 20, somewhere between 20 and 60 microseconds and  
15 because of that, the charge quantity, the electrical  
16 energy contained under the envelope or under the wave  
17 form for each pulse there is very low; its on the  
18 order of maybe 1.5 microcoulombs. Because you have  
19 such a small quantity of electrical energy in each of  
20 those pulses, you need a high voltage to drive the  
21 current across the skin or into the tissues. So  
22 that's why it's called high voltage; the high voltage  
23 devices allow you to adjust the voltage up to 500  
24 volts, but clinically that's never used; usually the  
25 voltage for wound healing is on the order of 75 to

00133  
1 maybe 200 volts.

2 In this type of current, there is a charge  
3 quantity, okay? And there are five papers, I only  
4 have four of them here, but there are five papers  
5 that describe how to compute, or actually describe  
6 the charge quantity that's delivered into the tissue.  
7 That charge quantity amounts to a dosage of charge  
8 that's delivered into the tissue. So, the way that  
9 charge is derived is simply determining how much  
10 charge occurs in each one of those pulses,  
11 multiplying it times the frequency, and that allows  
12 you to derive the total charge per second or per  
13 minute or per hour, and usually it's reported charge  
14 quantity per second. In these studies, the charge  
15 quantity varies somewhat, there's a window of charge,

16 okay, and that window of charge falls between 200 and  
17 600 microcoulombs of charge, do that's the dosage  
18 that you will see.

19 The other type of current is monophasic  
20 pulse current, okay? These are both pulse current,  
21 the one you previously saw as well as this one. The  
22 charge quantity can be 200 to 600 microcoulombs of  
23 charge, can also be delivered with this type of a  
24 more rectangular waive form.

25 So the main point I want to make is that

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1 it really comes down to when you review the papers,  
2 that it's the dosage of electrical charge that's  
3 delivered into the tissue, and it doesn't really  
4 matter whether the wave form is triangular,  
5 rectangular, or biphasic or monophasic, okay? What  
6 really counts is the quantity of electrical charge  
7 that ends up being delivered into the wound, and that  
8 window of charge is usually between 200 and 600  
9 microcoulombs per second. Thank you.

10 DR. GARBER: Maybe, this is sort of a  
11 technical issue and I don't know if we will have time  
12 free to return to it later. I'm wondering if the  
13 rest of the panelists would like to ask questions of  
14 Dr. Kloth now or wait until general questions. Yes,  
15 you have one now?

16 DR. OLECK: Just to follow up on that  
17 because it relates to some of the confusion I had  
18 with the ECRI specifications. Some of the things  
19 they listed under pulse current, they said were  
20 generated by a six-volt battery. Are you saying that  
21 has a longer pulse width or something?

22 MR. KLOTH: Well, the six-volt battery  
23 just energizes the device, okay, and then there are  
24 other components of the device that are able to  
25 increase the voltage appropriately and so the device

00135

1 is still, if it's a device used in the study, the  
2 device is still delivering that window of  
3 microcoulombs per second of 200 to 600 microcoulombs.  
4 And you know, that, I don't know if you're familiar  
5 with the old bone healing literature, but there was a  
6 window of charge in the early bone healing simulators

7 too, where they inserted a cathode into the fracture  
8 space and I believe it was something like, if they  
9 delivered 50 microcoulombs of charge, they saw bone  
10 healing, if they delivered more than 50 microcoulombs  
11 of charge, bone healing actually deteriorated. So  
12 there was a narrow window of charge there that was  
13 effective in the early bone healing studies.

14 DR. HOLTGREWE: In looking at the  
15 literature, it seems to me there's some variability  
16 in how you set the machine.

17 MR. KLOTH: There is.

18 DR. HOLTGREWE: My question is, how is it  
19 arrive upon where to set it? Is it trial and error?

20 MR. KLOTH: Well, it really comes down to  
21 a couple of things. One, the people who are doing  
22 wound healing with electrical stimulation with let's  
23 say a high voltage pulsed current device, usually set  
24 the voltage at between 75 and 150 volts.

25 DR. HOLTGREWE: How is that arrived at?

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1 MR. KLOTH: It's arrived at by adjusting  
2 the voltage upward until the patient, a sensate  
3 patient, perceives a tingling paresthesia in the  
4 perimeter of the wound. If they're insensate, you  
5 turn the voltage up until they get a muscle  
6 fasciculation, and then you turn it down until that  
7 muscle fasciculation disappears. In both cases,  
8 you're delivering a comfortable, a moderately strong  
9 but comfortable tingling paresthesia in the area of  
10 the wound, and they will have a range of as much as  
11 75 to 150 volts and the delivered voltage, you will  
12 be delivering 200 to 600 microcoulombs.

13 DR. HOLTGREWE: Does an increase correlate  
14 with better healing?

15 MR. KLOTH: I can -- well, it's  
16 interesting --

17 DR. HOLTGREWE: Because the bottom line  
18 here is to heal the wound.

19 MR. KLOTH: Exactly. I wanted to go back  
20 in Dr. Turkelson's report this morning, because he  
21 said they could find no difference in wound healing  
22 with direct or pulse current, okay? The reason I  
23 feel they couldn't deduct a difference was that it's

24 the charge quantity, and the charge quantity is the  
25 same whether you're using DC, pulse DC, or high

00137

1 voltage pulse current or you know, a rectangular wave  
2 form, or whatever, the pulse charge is the same. The  
3 variables are the voltage and frequency, and you can  
4 calculate charge regardless of what the voltage is  
5 and what the frequency is; if the frequency is 80  
6 pulses per second or 100 pulses per second, and the  
7 voltage is in that range of 75 to 100 volts, you will  
8 always come out with a charge quantity in that range  
9 of 200 to 600 microcoulombs.

10 DR. STANTON: Could you clarify something,  
11 because I think that I will paraphrase, and I wanted  
12 to make sure I understood what you said, because it's  
13 very powerful what you said, if it's true, and I'd  
14 like to understand where you came from in saying in  
15 your presentation, I think you said that it's the  
16 total charge that matters, not the wave form.

17 MR. KLOTH: That's correct.

18 DR. STANTON: And what's that based on,  
19 because in other physiologic responses to electrical  
20 stimulation, wave form matters a lot. Why do you say  
21 that for wound healing?

22 MR. KLOTH: Well, in the other  
23 physiological responses to electrical stimulation,  
24 such as, you are probably referring to neuromuscular  
25 electrical stimulation where you elicit a muscle

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1 contraction, or you're using electrical stimulation  
2 for pain suppression, you know, you're also  
3 delivering a charge quantity in both of those  
4 instances. The charge quantity for eliciting a  
5 muscle contraction is much higher than charge  
6 quantities of 200 to 600 microcoulombs, and it's also  
7 higher for pain suppression, depending on what device  
8 you're using and the stimulation mode for doing TENS.  
9 So, I don't know if that answers your question or  
10 not.

11 DR. STANTON: No, it doesn't. Let me  
12 rephrase then. Is there any experimental evidence  
13 that shows that there's no difference in wave form,  
14 that it's total charge delivered that makes the

15 difference?

16 MR. KLOTH: There is no experimental  
17 evidence, but it's the calculation that's easily done  
18 by taking one of those two wave forms, for example,  
19 that one or that one, and knowing the frequency and  
20 the duration. Actually, the formula is right there  
21 for this particular wave form. You know the area of  
22 one phase, that equals the phase charge. How do you  
23 come up with that? Well, because that's a triangular  
24 wave form, you take one-half of the phase duration  
25 times the amplitude, okay? In this case, the example

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1 is 20 microseconds, one-half phase duration is 20  
2 microseconds, times .35 amps or 3.25 microcoulombs,  
3 so the total charge per second then ends up being 342  
4 microcoulombs per second.

5 DR. GARBER: I think the question is not  
6 how you calculate it, the question is, how do you  
7 arrive at the conclusion that it's the total charge  
8 per second that matters and that the mode of delivery  
9 whether it's pulsatile or flat or whatever is  
10 irrelevant? That's your question, right, Marshall?

11 And so, are there animal studies or  
12 something that enable you to determine that whatever  
13 device you use, and you described where you go to a  
14 point where the patient really feels it, but that  
15 doesn't matter what device you use, you will always  
16 get equivalent results for wound healing. What is  
17 the basis for that statement?

18 DR. HOLTGREWE: Or to put it another way,  
19 is it like stretchy socks, one size fits all, it  
20 doesn't really matter where you set the machine?

21 DR. GARBER: As long as you get the same  
22 total charge?

23 MR. KLOTH: It doesn't matter where you  
24 set the machine, as long as the sensate patient is  
25 feeling this moderately strong tingling paresthesia.

00140

1 The wave form doesn't seem to matter.

2 DR. STANTON: Another way of looking at  
3 that, has anybody looked at the literature and gone  
4 and seen whether the separation in studies that seem  
5 to have an effect and those that don't, that they

6 shake out by the charge that's delivered?

7 MR. KLOTH: No, I don't think anyone has  
8 gone to the literature. As I said, these five papers  
9 basically describe pretty much that same window of  
10 charge, but I see your point, it would be good to go  
11 back and look at the other papers that didn't  
12 describe the charge quantity to see if wound healing  
13 was better or worse.

14 DR. SIGSBEE: Just to follow up on this  
15 area a little bit further, is it that there is no  
16 evidence that distinguish between different methods  
17 of delivering a charge, or do you think the evidence  
18 supports the fact that the method of delivering a  
19 charge is irrelevant, the pulse wave form?

20 MR. KLOTH: I think the wave form is  
21 irrelevant.

22 DR. SIGSBEE: You think, but what's the  
23 evidence that supports your thoughts?

24 MR. KLOTH: There is no hard evidence.

25 DR. SIGSBEE: All right.

00141

1 DR. OLECK: Does the alternating current  
2 in those pulse electromagnetic field items, do they  
3 deliver a net charge to?

4 MR. KLOTH: Yes, they do. Alternating  
5 current we said is sinusoidal wave form, and in a  
6 pulse electromagnetic field device, what is done is  
7 they increase the frequency all the way up into the  
8 megahertz range, and usually those devices are  
9 delivering 27 megahertz, and 27 megahertz is the  
10 frequency, and that's an electromagnetic field that  
11 is inducing the current in the tissues. We don't  
12 have evidence of the charge quantity that is  
13 delivered by that method.

14 DR. OLECK: So you can't really calculate.

15 MR. KLOTH: Right. The supposition is the  
16 three or four studies that have been done with that  
17 form of electromagnetic field of energy report  
18 favorable outcomes, that the charge quantity is  
19 probably favorable, okay, but we don't know what it  
20 is.

21 DR. GARBER: Thank you. Let's move on to  
22 the next public speaker.

23 MS. CONRAD: Thank you, Mr. Kloth.  
24 Dr. Cavorsi.  
25 DR. CAVORSI: Thank you. Good afternoon.

00142

1 While listening to all that expert testimony this  
2 morning, I became somewhat concerned over hearing all  
3 that testimony concerning the effectiveness of  
4 electrostimulation with, in the use of pressure  
5 ulcers, that my fear is that this panel may  
6 erroneously conclude that electrical stimulation  
7 should be used only for electric stimulation.

8 As clinical director of, again, a large  
9 wound care center, I treat a lot more patients than  
10 just pressure ulcerations. I use electrical  
11 stimulation to treat all nonhealing chronic wounds.  
12 And I would advise that electric stimulation is  
13 extremely effective in chronic wounds, regardless of  
14 etiology. As I previously stated, in my experience,  
15 regardless of the etiology, which is usually  
16 addressed during the treatments with standard  
17 protocols, some of these patients still do not  
18 respond. Because of the lack of research data or  
19 literature concerning patients with diabetic ulcers  
20 or ischemic ulcers, that does not mean that in  
21 clinical practice, electrical stimulation does not  
22 benefit these patients, it does. How it does it, how  
23 does it do it, there's really no literature to  
24 indicate how that works.

25 It was mentioned earlier that electric

00143

1 stimulation changes the polarity and transfers itself  
2 to the wound site. That may be one of the reasons  
3 why it heals a chronic wound. I wish it were that  
4 simple, it's not that simple. I think these patients  
5 have wounds that become quiescent and no longer  
6 respond. It was interesting, even if you try and  
7 correct the underlying cause, it was interesting to  
8 see this morning, that it was shown that electric  
9 stimulation actually initiated the response in  
10 fibroblast to produce transforming growth factor beta  
11 and as we well know, growth factors in wound healing,  
12 there's a tremendous body of knowledge out there  
13 today that indicates it is extremely important.

14           It may show later, perhaps later, that  
15 electric stimulation might either stimulate those  
16 receptor cells on the target cells, or might do  
17 something similar to that effect. But the point I'm  
18 trying to make is, electric stimulation responds or  
19 heals and is effective in chronic wounds, not just  
20 pressure ulcers. And again, it would be devastating  
21 to my practice if I could only use this modality in  
22 patients with pressure ulcers.

23           I would love to put some clinical trials  
24 together for you for an arterial ulcer. You saw it  
25 clinically this morning, that we can heal a severely

00144

1   arterial ischemic ulcer. How do you do that? How do  
2 you get a patient with severe popliteal disease, who  
3 has a limb threatening lesion, who is  
4 nonreconstructable, who has severe pain, and put that  
5 patient in a clinical trial? It just can't be done.  
6 There are just some things we can't do with clinical  
7 trials, and you have to sort of trust the clinicians  
8 that are out there doing this thing. And I just  
9 wanted to address that point. Thank you.

10           DR. HOLTGREWE: Let me ask you a question.  
11 When you're treating different types of ulcers, do  
12 you set the machine at the same setting on all three  
13 or do you change it?

14           DR. CAVORSI: I have no idea because I do  
15 not touch those machines. I am not a physical  
16 therapist, this is a physical therapy modality.

17           DR. HOLTGREWE: What does the physical  
18 therapist do?

19           DR. CAVORSI: You would have to ask the  
20 physical therapist. Those are technical questions  
21 that I cannot answer, and I wouldn't be answering  
22 truthfully if I tried.

23           DR. ZENDLE: You said that you find it  
24 valuable no matter what the etiology of the ulcer in  
25 recalcitrant nonhealing ulcers?

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1           DR. CAVORSI: Correct.

2           DR. ZENDLE: Would you advocate limiting  
3 the use of electrical stimulation to only nonhealing  
4 recalcitrant ulcers, or would you use it on every



5 ulcer?

6 DR. CAVORSI: I tend to use it on every  
7 ulcer.

8 DR. ZENDLE: Why?

9 DR. CAVORSI: Again, based on that  
10 experience that I've had in the past. Remember, I  
11 mentioned initially, I only used it in patients who  
12 did not respond to standard therapy. After a while,  
13 I realized or learned that these patients are  
14 actually healing better and faster, and I no longer  
15 held that treatment based on that observation.  
16 That's a clinical observation on my part, and only on  
17 that. I can't give you literature to base that on,  
18 but on my clinical observations, these patients who  
19 were getting standard of care only and those patients  
20 -- and were healing -- and those patients who were  
21 getting standard of care with the addition of  
22 electric stimulation were doing it better and were  
23 doing it faster.

24 DR. ZENDLE: And what stage, for those  
25 patients that you haven't just limited to nonhealing,

00146

1 are you using electrical stimulation on all four  
2 stages of ulcers?

3 DR. CAVORSI: On all types of wounds?

4 DR. ZENDLE: No, the stage of the ulcer.  
5 Are you using only Stage III and IV, are you using  
6 Stage II, III and IV?

7 DR. CAVORSI: Well, there is really no  
8 significant indication to use electric stimulation in  
9 patients with a Stage I pressure ulcer, or even a  
10 noncomplicated Stage II pressure ulcer. We would  
11 only use it for Stage III and Stage IV, because  
12 that's the only type of ulcer that really requires  
13 this type of treatment, more aggressive treatment,  
14 more proactive treatment, because other ulcers  
15 wouldn't even come into play. I wouldn't even  
16 consider it.

17 DR. ZENDLE: That's what I wanted to know,  
18 so you would just say Stages III and IV?

19 DR. CAVORSI: And/or recalcitrant Stage  
20 II, one that's just Stage II, a partial thickness  
21 pressure ulcer which does not respond to the usual

22 standard therapy, yes, I would use it.  
23 DR. ZENDLE: And if I understand what  
24 you're saying, these Stage II ulcers, they have to be  
25 recalcitrant, not responding to the standard

00147

1 treatment, before you would use electrical  
2 stimulation?

3 DR. CAVORSI: That is correct, that is my  
4 personal bias, that's correct.

5 DR. SIGSBEE: A couple of questions. You  
6 mean to tell me that somebody is using a therapy on  
7 your patients and you don't know what it is, that is,  
8 the settings of the machine, the type of wave form,  
9 the duration of therapy?

10 DR. CAVORSI: Yes. I know my physical  
11 therapist, I know exactly what they're using.

12 DR. SIGSBEE: That was the question; what  
13 are they using?

14 DR. CAVORSI: That's not what I heard.

15 DR. SIGSBEE: No, no. That's what we're  
16 talking about. You're coming here presenting your  
17 personal experience in your wound care center. What  
18 are your physical therapists doing for different  
19 types of wounds?

20 DR. CAVORSI: Yeah. We use a high volt  
21 pulsed current in our patients, and I can tell you  
22 they use 150 volts of power. I mean, that I can tell  
23 you, because that's written. I don't understand all  
24 the physiology involved, you know, let me say the  
25 physics part of it as well as they do, okay? That's

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1 the truth.

2 DR. SIGSBEE: I'm just a little bit  
3 curious, and I don't have any involvement with wound  
4 care. You run a wound care center; is that correct?

5 DR. CAVORSI: That's correct.

6 DR. SIGSBEE: Can physical therapists bill  
7 independently for what they do compared to your  
8 professional services?

9 DR. CAVORSI: Can physical therapists bill  
10 independently?

11 DR. SIGSBEE: For their wound care  
12 services?

13 DR. CAVORSI: Yes.  
14 DR. SIGSBEE: They can. And do they in  
15 your center?  
16 DR. CAVORSI: No.  
17 DR. SIGSBEE: They don't.  
18 DR. HOLTGREWE: Well, my question was,  
19 this technology is advocated for three basic types of  
20 wounds, and my question was, is the setting on the  
21 machine different for the three wounds or is it the  
22 same for all three?  
23 DR. CAVORSI: I don't know.  
24 DR. HOLTGREWE: You don't know?  
25 DR. CAVORSI: I can't answer that.

00149

1 DR. HOLTGREWE: Who makes the decision,  
2 the therapist makes the decision?  
3 DR. CAVORSI: The physical therapist has  
4 very specific protocols.  
5 DR. HOLTGREWE: Based on what, what  
6 criteria do they use to set the machines?  
7 DR. CAVORSI: I don't know that.  
8 DR. HOLTGREWE: Who would?  
9 DR. CAVORSI: The physical therapist.  
10 DR. ZENDLE: Maybe we should ask a  
11 physical therapist.  
12 MS. UNGER: This is a physical therapist,  
13 and I would be love to be able to tell you what's  
14 going on. Basically in the clinic that I work in, we  
15 have a standard protocol that's set up where we treat  
16 the patient initially with negative polarity and then  
17 switch the patient to positive polarity. You're  
18 asking me how many votes I put into the machine?  
19 DR. HOLTGREWE: Stop. Upon what do you  
20 base that policy?

21 MS. UNGER: I base that initial policy on  
22 the literature way back in the 1960s and 50s that  
23 talked about low intensity direct current and the  
24 polarity effects on wound healing with the use of  
25 those different type of parameters. And I've used

00150

1 that since 1980 to treat patients.  
2 I think the key factor is, again, after  
3 looking at these studies and certainly researching

4 everything about high volt that I could find, about  
5 electrical stimulation for wound healing, certainly  
6 the numerous times that I myself have gone to HCFA  
7 and said let's look at this thing and see how  
8 effective it really is on patients, we have looked at  
9 total charge, you know, does it matter if it's  
10 monophasic or does it matter if it's a biphasic wave  
11 form, and people get real confused with that issue.  
12 But when you start looking at the research, studies  
13 that are out there, and start looking at what wave  
14 form was it, what was the pulse duration, what was  
15 the pulse width, and calculate out your total charge,  
16 almost all of those studies fit into that total  
17 charge window that Mr. Kloth talked about.

18 Where we find that we change with  
19 different patients is, I happen to use a particular  
20 device that reads peak output on a patient.  
21 Certainly if I place electrical stimulation on you,  
22 versus placing it on myself or anybody else sitting  
23 in the room, your body may respond differently to  
24 that electrical stimulation than mine does. It may  
25 take an actual increase in voltage to get the right

00151  
1 amount of current going into the tissues, and I judge  
2 it from that perspective.

3 DR. HOLTGREWE: How do you make that  
4 determination?

5 MS. UNGER: I make that determination by  
6 reading as my peak output is where my voltage is  
7 reading. The particular device I use, I can dial in  
8 voltage and then I can check to see --

9 DR. HOLTGREWE: No, I understand, but  
10 what's the relationship between this and efficacious  
11 response in wound healing? How do you know?

12 MS. UNGER: Well, I want to make sure that  
13 the patient is getting that total amount of charge.

14 DR. HOLTGREWE: So the bottom line is, the  
15 more charge you put in, the better the effect?

16 MS. UNGER: No, I can't answer that.

17 DR. HOLTGREWE: That's essentially my  
18 question.

19 MS. UNGER: I know that's your question,  
20 but I think what you have to remember, and I can only

21 ask you to please think about this, we're talking  
22 about the human body, and the human body responds  
23 very very differently depending on those  
24 variabilities of diagnoses, comorbidities, the  
25 patient's body responds very differently and we know  
00152

1 this in medical practice. One patient responds very  
2 differently to one pain medication versus another.

3 So when I place electrical stimulation on  
4 patient A, I'm able to dial in 100 volts and I may  
5 get a peak output that reads 100 volts. Patient B, I  
6 may have to dial in 150 volts to get 100, or 500  
7 milliamps of current. And I do that by looking at my  
8 patient on an individual basis saying these are the  
9 parameters for my protocol, and in the last 20 years  
10 I've gotten very tremendous results with electrical  
11 stimulation, and that's what I base it on.

12 DR. HOLTGREWE: Okay. Well, that last  
13 statement maybe helps me in that you use your  
14 previous experience to determine, where with  
15 antibiotics for instance, there's a range of therapy.  
16 There's a point at which you don't give enough  
17 antibiotic you get no favorable response, you give  
18 too much, you get into a toxic profile. But I guess  
19 one of my things I don't understand in this is where  
20 do you set the machine, because there seems to be a  
21 substantial variation in the literature I've read.  
22 And I just wondered how you as a therapist decide  
23 whether or not the patient is getting enough or too  
24 much voltage. Do you give them as much as they can  
25 tolerate?

00153  
1 MS. UNGER: No. You turn your intensity  
2 up until you see a slight twitching of the patient.

3 DR. HOLTGREWE: Yeah, but is that  
4 associated with better wound healing? That's my  
5 question.

6 MS. UNGER: Well, if I had a subliminal  
7 response from the patient, certainly I might see  
8 less. I don't use that. I can't tell you it relates  
9 to less healing, because I don't use it in my clinic.

10 DR. HOLTGREWE: Yeah, I guess that's my  
11 problem is that I don't see a correlation between how

12 much energy you put in and the response. I think  
13 that's my question.

14 MS. UNGER: Well, I guess if we took apart  
15 -- you know, these questions have been raised where  
16 somebody's talking about the scientific evidence, and  
17 I think if I took every one of those studies that's  
18 out there, identified the piece of equipment that was  
19 used, identified the parameters and then took the  
20 total charge that was offered to the patient by those  
21 parameters, I might be able to ask the question that  
22 was asked here, did those patients that didn't  
23 respond have less charge than those patients that did  
24 respond? I don't know that now, because that  
25 question hasn't been asked before. And

00154

1 unfortunately, the frustrating part of being a  
2 clinician is, I have a very difficult time when I  
3 know a particular treatment is very effective for  
4 intervention, and certainly if you look at the  
5 baseline outcome in all of these studies, most of it  
6 is 2.4 times faster healing. Why would I not use it  
7 on a patient? Why wouldn't I move them to a better  
8 point in their life? Why wouldn't I make them more  
9 independent?

10 I guess my other thought is that it's very  
11 difficult without looking at a wound -- if I put  
12 electrical stimulation on a wound and in five days I  
13 don't see pink tissue or necrotic tissue loosening  
14 and having autolytic properties going on, I don't see  
15 a red healthy wound bed, I'm not doing right for my  
16 patient. But those are clinical observations, and I  
17 would change my parameters at that point in time.

18 DR. SIGSBEE: Let me, and I don't want to  
19 belabor the point, but the decision on how much  
20 current to deliver here, and this covers several  
21 speakers, has sort of been determined that this is an  
22 end point where you either get tingling or muscle  
23 twitching, and then back it off a little bit from the  
24 muscle twitching, and that's just sort of been the  
25 standard, there is no present good evidence that

00155

1 that's the right amount of current to deliver, it's  
2 just the way it's been done, and it's thought that

3 that is at least one way of determining at least an  
4 effective current; is that right?

5 MS. UNGER: That's correct; that's all the  
6 way back to, I believe it's 1934 that we saw a study  
7 that said that, and that's what we based it on.

8 DR. SIGSBEE: You're commenting on your  
9 own personal experience, and I wonder if that's the  
10 experience of other physical therapists in the room,  
11 is that this is how it is and there isn't good  
12 evidence as to what is the most effective mechanism.

13 DR. TURKELSON: I understand where you're  
14 coming from with that, and I think there is some  
15 evidence that shows the contrary, that we know from  
16 microcurrent studies, when patients are given these  
17 very very low level stimulations, they do not  
18 respond. On the other extreme, we do not know. And  
19 I think one reason we don't go to the other extreme  
20 is we don't want the muscle contraction as a  
21 compounding variable, plus the fact that the skin is  
22 broken, resistance is decreased, and we're putting in  
23 possibly way too much current. And we're very  
24 concerned in PT not to overstimulate an area to cause  
25 an electrical burn, or things of this nature. So we

00156

1 do stay off it at a tingling paresthesia, to make  
2 sure that we are not giving too much stimulation to  
3 the patient that could cause harm. But if you go to  
4 the other extreme, too little stimulation will not  
5 work.

6 DR. GARBER: Let me just ask. Dr.  
7 Holtgrewe asked the question earlier about the use of  
8 different, do you try to set them differently for  
9 some other characteristics according to the cause of  
10 the wound, that is, whether it's diabetic or venous,  
11 or a pressure ulcer. And then you said in your  
12 comments before if I heard you correctly, that you  
13 take into account the underlying disease, et cetera.  
14 So, could you answer his question about that  
15 particular question? Do you use a different protocol  
16 or do you try to set anything differently according  
17 to whether it's a pressure ulcer or one of the other  
18 kinds of ulcers?

19 MS. UNGER: In my clinic it does not

20 matter what type of ulcer it is; the protocol is the  
21 same. The same parameters are there for negative  
22 polarity, the same parameters are there for positive  
23 polarity. What changes is, when I apply that machine  
24 to a patient and I don't read a peak output  
25 occurring, which for 100 volts on my particular

00157

1 machine, it would be 500 milliamps of current, and if  
2 my peak output doesn't reach 500 milliamps of  
3 current, I in fact up my voltage until I get 500  
4 milliamps of current.

5 Now, can I tell you that that is a case  
6 that is more medically compromised? I probably could  
7 make that assumption now. I have not ever recorded  
8 it so I can't tell you it's diabetic versus the  
9 arterial versus the pressure, I don't know that. I  
10 would make an assumption knowing the physiological  
11 processes that it may be that person that's more  
12 complicated, but I can't tell you that for sure. The  
13 protocols remain the same unless it's not reading the  
14 peak output of 500 milliamps.

15 DR. GARBER: All right. Mike Maves, and  
16 then Les is next.

17 DR. MAVES: Yeah, and I hate to kind of go  
18 back because I know we're trying to concentrate on  
19 clinical trials in where we're headed, but from the  
20 academics in physical therapy, has there been a dose  
21 response? I think what Dr. Holtgrewe is trying to  
22 find out is, is there a rationale for the amount of  
23 current or the voltage that is delivered? We heard  
24 from Dr. Frantz this morning that they haven't been  
25 able to quantify what the negative potential is on

00158

1 the skin, I guess it might be minus 23 millivolts.  
2 What's the dose response? Have you had an animal  
3 model or something where we've been able -- I hate to  
4 kind of go back to basic science, but I think that  
5 would help some of the questions up here if there  
6 were some references and some data to relate it to.

7 DR. ZENDLE: Actually, my questions's  
8 related so I'd like to ask it and you can answer them  
9 both together. And that's in addition to his  
10 question about the dose, what about the frequency?



11 How often or how long? Is it every day, is it three  
12 times a week, is it for a half hour, six hours, is it  
13 continuous? Can you respond to how those decisions  
14 are made?

15 DR. FRANTZ: Let me make a few general  
16 comments as an academic nonphysical therapist nurse,  
17 but wound healing academic person and just say that  
18 part of the difficulty in responding to the kind of  
19 questions you're asking us for chronic wound patients  
20 is that we don't have a chronic wound model, and that  
21 has hindered us tremendously in terms of laboratory  
22 research. In the last decade in particular, we have  
23 a much better understanding that acute wounds behave  
24 very differently than chronic wounds, and that our  
25 assumptions of two decades ago that we could

00159  
1 extrapolate the acute wound data to chronic wound  
2 populations, we know we can't do that anymore, so we  
3 don't do that anymore.

4 We don't take the burn literature and move  
5 it to chronic wound care. So until we have that  
6 animal model to do the kind of controlled studies  
7 that we need to do of all those confounding  
8 variables, it makes it very very difficult, and there  
9 are people actively working on that model, but nobody  
10 has done it.

11 We also know, and I know some of the  
12 people in this room, Dr. Oleck, I think you were at  
13 the FDA meeting a couple of years ago, where the FDA  
14 struggled to look at study design for wounds, and we  
15 spent a day and a half sitting there looking at all  
16 the variables, and we couldn't even come up with a  
17 consensus of opinion on what the standard controls  
18 should be for those studies, because the reality is  
19 that if you look at a venous ulcer patient, that's  
20 one set of controls, and adjunctive therapies that  
21 you need to be evaluating, versus pressure ulcer,  
22 versus venous ulcer, versus all the other kind of  
23 chronic wounds. So it's tremendously complicated,  
24 and so as you pose these questions, part of the  
25 reason that my colleagues can't give you any answers

00160  
1 is because we don't have an arena in which to do the

2 research yet, and yet, we have to take care of  
3 patients every day.

4 DR. MAVES: Excuse me, but has anything  
5 been done on patients where you take a series of  
6 patients with pressure ulcers and somebody gets 25  
7 microvolts, somebody gets 50, somebody gets 74 and  
8 somebody gets 100, and kind of just look at that  
9 then? I understand your concern about not having an  
10 animal model, that certainly hinders that, but has  
11 anything been done clinically to sort of determine  
12 what's the most effective dose?

13 DR. FRANTZ: I'll let my colleagues in  
14 physical therapy answer that, but let me just call to  
15 the table significant evidence that's coming out from  
16 the most controlled trials of platelet drive growth  
17 active beta, the Greenwich trials, that are probably  
18 the largest group trials that we've ever had in the  
19 history of wound healing, probably the best  
20 controlled by the FDA, and we know that the results  
21 now for the second phase, where they are looking at  
22 the same product in pressure ulcers, is beginning to  
23 suggest a different outcome than it was in diabetic  
24 neuropathic ulcers, so -- and that's thousands or  
25 millions of dollars later.

00161

1 MR. KLOTH: I will try to answer your  
2 questions about the dosage. There are no studies  
3 comparing say 50 microvolts or 50 milliamps or 50  
4 microcoulombs against 500 microcoulombs or 500  
5 microamps, or 500 volts, there are no studies, we  
6 need those studies. But, the convincing evidence  
7 lies in the fact that we have the clinical trials as  
8 I said before, that demonstrate accelerated healing  
9 using that window of charge in the range of 200 to  
10 600 microcoulombs, and we arrive at that based on  
11 patient perception of tingling paresthesia, and a  
12 combination of voltage and frequency.

13 DR. GARBER: Dr. Kloth, maybe -- I'm  
14 hoping we can move on soon, but I just want to ask if  
15 I'm correctly summarizing your view of this, and that  
16 is, that the levels that are used are the ones that  
17 have been tested and proven effective, and we don't  
18 have direct studies about whether those levels are

19 optimal yet, but we do have studies showing that  
20 these levels work. Would that be a fair summary?

21 MR. KLOTH: That is correct. Someone else  
22 had a question about how often we do this. Some  
23 folks do -- most of the time it's one hour a day.  
24 Some people do five days a week, some people do seven  
25 days a week. There are no studies indicating that

00162

1 seven days a week are better than five days a week.

2 DR. ZENDLE: How about once a week?

3 MR. KLOTH: No, there are no studies where  
4 it was done once a week. The studies were either  
5 five days or seven days, one hour a day.

6 MS. UNGER: I think what you will see in  
7 clinic situations if you just went out and polled all  
8 of the therapists, nurses that may be involved in  
9 clinics where electrical stimulation is done, on an  
10 outpatient basis I think you see a minimum frequency  
11 of three times per week, and certainly on the  
12 inpatient side of things, acute care, skilled nursing  
13 or rehab site, you would see a maximum of seven times  
14 per week. So I think your frequency rate is  
15 somewhere from three to seven times a week, and I  
16 think that has to do with the acuity level of the  
17 patient. When you get a patient that's outpatient to  
18 come into your clinic three times a week, there may  
19 be some more things the patient can do with reference  
20 to exercise and off-loading and those kinds of  
21 things, where a patient who is acutely ill that's  
22 hospitalized, may have far more intervention. I  
23 don't think we've done any studies that have actually  
24 compared what's the minimum amount to get response.  
25 Nobody has compared one time a week to two times a

00163

1 week, to three times a week, to seven times a week.

2 DR. OLECK: One of the things, just to get  
3 a little different track here, we've talked and a lot  
4 of the discussion today has been focused on the idea  
5 that these are being done in a facility setting. So  
6 from my perspective from the contractor, I know that  
7 we will be getting a number of claims advocating use  
8 in the home setting, and I just wonder whether we can  
9 get some comments from people about the various types

10 of devices, whether they are safe. You know, some of  
11 these where you are applying electrodes directly to  
12 the wound, I guess I have more questions about that,  
13 about whether that would be safe in the home setting,  
14 and that kind of ties into this other question about  
15 how often to treat or how long to treat. Certainly  
16 some of the constraints, I'm sure the fact of how  
17 often you can reasonably get the patient to come into  
18 the outpatient clinic, but at home, I guess they  
19 could wear these for long periods of time or use them  
20 for long periods of time. Are there any comments  
21 about use of these in a home setting?

22 MS. UNGER: I have some personal comments,  
23 so I'll start first and if you want to follow, please  
24 do. My personal opinion is that there are some  
25 patients, limited, but some patients and patient's

00164

1 families that can be taught how to appropriately  
2 apply electrical stimulation. I would say high  
3 voltage pulse, because that's what I prefer to use  
4 for my patients. I also think that that assures me  
5 that the patient cannot burn themselves if it would  
6 be left on too long. I think the real issue with it  
7 is if you have a wound that really requires  
8 intervention, I question how often the skilled  
9 professional may need to assess that wound, so the  
10 patient continues to progress in a timely fashion.

11 I think the other issue, even though I  
12 hate to say that reimbursement drives a lot of what  
13 happens clinically, right now a patient would have to  
14 pay to either rent or pay out of pocket for that  
15 particular device to be used at home, because right  
16 now I believe the coverage decision still remains,  
17 chronic or intractable pain for a home stimulator.  
18 So unless the patient presented with that diagnosis  
19 in combination with a wound, the patient would have  
20 to pay out of pocket, which many of our Medicare  
21 patients will not do. So, I think that limits how  
22 much it will be used at home.

23 DR. OLECK: Well, we're talking about a  
24 potential change in coverage here, and if it was  
25 covered in the home setting, do you have any problems

00165

1 with most people leaving your clinic and just being  
2 given one of these devices by the supplier to use at  
3 home?

4 MS. UNGER: I have no problem with that  
5 being done as long as the patient is capable of doing  
6 that, and I think there are some real questions as to  
7 whether the patient would always be capable of doing  
8 that. I think the other issue clearly would be what  
9 I would call an acuity or severity level of what the  
10 patient's, you know, external circumstances may be  
11 related to certain comorbidities. There may be some  
12 things as a physician. I mean, I know just with the  
13 physicians that we work with, they would halt that in  
14 a number of situations where they wouldn't feel the  
15 patient could appropriately assess the condition. So  
16 I think there would be some limitation where that's  
17 concerned. Could you teach a patient at home to do  
18 it, I certainly think you could. You teach a patient  
19 how to do a TENS unit at home, and it's pretty much  
20 the same thing.

21 MR. KLOTH: And if the patient is followed  
22 by home health care, nurse or physical therapist on a  
23 weekly basis, to make sure that they are following  
24 the protocol, or when they come into the clinic, to  
25 double check that they are following the protocol,

00166  
1 there shouldn't be a problem.

2 DR. SIGSBEE: Okay. Just one follow-up  
3 question. We have talked about, obviously our charge  
4 is to try to look at the evidence and comment on the  
5 evidence, and the coverage issue is really HCFA's  
6 decision. One of the things that we have sort of  
7 spoken around today but not really talked about is  
8 the comparison of electrical stimulation with other  
9 some of the newer modalities in management of wound  
10 care, specifically some of the gels and the absorbent  
11 beads, and some of the other things that are even now  
12 being understood in advance. And I wonder if anybody  
13 would be willing to --

14 DR. GARBER: Let me ask that we hold that  
15 off for the general discussion later, because we have  
16 a lot of issues. Let's move on to the third public  
17 speaker.

18 MS. CONRAD: The final speaker,  
19 Dr. Spielholz.

20 DR. SPIELHOLZ: I just wanted to revisit a  
21 comment that I had made before about the ECRI comment  
22 that looking at the sense of wounds healed over a  
23 short period of time may be a flawed outcome measure,  
24 and then Dr. Turkelson's concern may rebut what I'm  
25 saying.

00167

1 But let me just refresh your memory on  
2 this. If you have the ECRI report in front of you,  
3 on page 84, the section begins, many wound healing  
4 studies report the number and/or percentage of  
5 patients healed at given time intervals. One might  
6 assume that this is a straightforward simple  
7 measurement of the therapy to promote healing.  
8 Unfortunately, the number or percentage of patients  
9 healed is a flawed outcome measure because it depends  
10 on study follow-up duration and initial wound size.

11 What I have copied here just in case you  
12 don't have the ECRI report, is that ECRI then goes on  
13 to give an example of why looking at wounds healed  
14 over a particular period of time may be a flawed  
15 outcome measure, and basically, you tell me if I  
16 interpret this wrong, basically they're setting up a  
17 situation where there are two groups, A and B, and as  
18 you see on the slide, they have a particular  
19 distribution of wound sizes. In group A -- both have  
20 15 patients in them and if you look at the means and  
21 standard deviations of the wound sizes, the means and  
22 standard deviations are the same, so they can still  
23 have different wound sizes, but the means come out to  
24 be the same. The distribution is different in that  
25 group A, which is going to be the treated group, has

00168

1 some wounds that have an area of 6 square  
2 centimeters, whereas group B, which is going to be  
3 the control group, has 8 square centimeters as their  
4 smallest number. Okay?

5 Now, ECRI then goes on and says down  
6 there, further, the next paragraph says, if the  
7 experimental and standard therapies both had linear  
8 healing rates of 1 square centimeter per week, then

9 at the end of six weeks, basically what would happen  
10 is that those patients in the group A that had 6  
11 square centimeter ulcers would heal, because they had  
12 been healing at a rate of 1 square centimeter per  
13 week, at the end of six weeks those would have  
14 healed, but nothing or none in group B would have  
15 healed, because their smallest ulcers were 8 square  
16 centimeters.

17 So you can see that they could have the  
18 same healing rate, that the E-stim was really not  
19 making the difference is what ECRI is implying here,  
20 yet, it would appear that the E-stim was having a  
21 difference because those patients healed sooner. So  
22 when we come along and say well, we saw them in seven  
23 weeks, all these patients healed in the stim group  
24 and they didn't heal in the control group, you're  
25 saying that could be a flawed outcome measure.

00169

1 The problem with this assumption is that  
2 both groups have a linear healing rate of one square  
3 centimeter per week, so it would take the larger  
4 ulcer longer to heal. So let's assume that they  
5 started healing one square centimeter per week after  
6 being placed into the treatment groups. I redrew the  
7 ECRI healing rates here, and basically what you see  
8 if for the two groups, it decreasing in size over the  
9 first six weeks, and at the end of the six weeks, one  
10 would have healed totally, the other group still  
11 would not have healed, but as you can see, there are  
12 healing rates that are measurable. Is this reality?  
13 That's my question. How much reality is this?

14 Let us have the next slide please, the  
15 next overhead. And let's just look at these examples  
16 to see whether this is reality. In the Kloth and  
17 Feedar group, which I showed you before, in this  
18 situation at the top, all patients, all nine patients  
19 at the end of seven weeks healed. In the control  
20 group, however, there was not that type of a linear  
21 drop. In fact, if you look at the statistics of the  
22 control group, the control group if anything, got  
23 bigger, by about 6 percent. So there was no  
24 concomitant drop that you would have to see if the  
25 healing rates were indeed linear the way ECRI

00170

1 proposes.

2 Can we have the next slide please? So,  
3 that ECRI model does not mimic reality in this  
4 situation. This is from the study of Wood et al.,  
5 where again, they plotted the healing rate over time  
6 and as you can see, one of them is going down very  
7 nicely, that's showing the decrease in the percent of  
8 the wound that is remaining, whereas the other line  
9 is the control group and it is certainly not  
10 following a linear drop the way ECRI suggests.

11 So therefore, I would argue that the ECRI  
12 argument that healing over a period of time is a  
13 flawed outcome measure is flawed because the basic  
14 assumption does not follow what reality is. Thank  
15 you.

16 DR. ZENDLE: Isn't that may be a flawed  
17 outcome?

18 DR. TURKELSON: Yes. We never said that  
19 wound healing rates were inappropriate outcome  
20 measures. This was an example that illustrated that  
21 linear wound healing rates are probably  
22 inappropriate. As a matter of fact, the chief  
23 outcome measure that we used is an exponential model  
24 of wound healing rates. Wound healing rates are out  
25 outcome measure. The linear model that I think, one

00171

1 can show a hypothetical situation, I think the  
2 arguments made here actually prove my point, the  
3 linear model clearly doesn't fit the data, and that  
4 was our point.

5 Also, I question whether the argument is  
6 even important. The question here really is, you  
7 know, we have data that suggests that the exponential  
8 model fit all of the data we could get at hand. We  
9 could niggle over whether the rates are linear or  
10 not. I don't see data that the wound healing rates  
11 are linear. I think the argument here is that they  
12 are not and I would agree with that wholeheartedly,  
13 they clearly are not. Hypothetically, theoretically,  
14 linear wound healing rates can't work. That's why we  
15 used exponential wound healing rates as the primary  
16 outcome measure.



17 DR. GARBER: Let me suggest that we defer  
18 further discussion of the linearity issue until,  
19 unless and until it becomes germane to the  
20 deliberations of the committee.

21 I would like to call on John Whyte from  
22 HCFA, who has a few comments.

23 DR. WHYTE: I think Dr. Garber wanted me  
24 to go over very briefly Appendix A, which were the  
25 articles reviewed since the ECRI report, and I'll

00172  
1 just give you a very brief synopsis and then if you  
2 like, we can go over each article very briefly and  
3 then if you have any questions, I can answer them or  
4 you can continue that as part of your deliberations.

5 As I mentioned this morning, since the  
6 ECRI report, we have continued to do work on this  
7 topic and what we decided to do was search the  
8 literature since the update in 1997, and we set very  
9 broad search parameters. Essentially we used the  
10 terms electrical stimulation and wounds, because we  
11 wanted to include as much information as possible.  
12 This would not necessarily be our normal operating  
13 principles, because normally when we do our  
14 literature search we like to look for controlled  
15 trials, whether it's an historic control, perspective  
16 control, or a retrospective control, but in this  
17 situation we wanted to include as much information as  
18 possible.

19 What that yielded was Appendix A, which  
20 were a total of 17 articles. Not all of those were  
21 studies. There were six case series, there were five  
22 randomized clinical trials, there were four  
23 literature reviews, there was one meta-analysis, and  
24 there was one opinion article. And you should note  
25 that three of the 17 articles were not published and

00173  
1 ones was an abstract, and we would normally not  
2 include those as part of a systematic literature  
3 review with strict inclusion criteria, but in this  
4 situation we did want to be as broad as possible to  
5 present all the information to you and allow you to  
6 decide how you wanted to weigh that information.

7 We can go over briefly and just in summary

8 of the six case series. I know Dr. Turkelson talked  
9 earlier this morning about that, to take a certain  
10 number of studies and talk which are statistically  
11 significant and which aren't. I'm just going to  
12 mention it to you in summary and then go over each  
13 one and you can decide how you want to look at it.

14 But of the six case studies, two of those  
15 had statistically significant results, four of those  
16 did not provide enough statistical information to  
17 determine whether or not the data was statistically  
18 significant. And of the five randomized clinical  
19 trials, three were not statistically significant and  
20 two were statistically significant, although you do  
21 have to look at the articles to see exactly what they  
22 were measuring.

23 And if you'd like, we can briefly go  
24 through the articles. The first two articles are by  
25 Baker, which essentially are companion pieces. They

00174

1 both appeared -- actually, excuse me -- one appeared  
2 in Diabetes Care, and one appeared in Wound Repair  
3 and Regeneration. Basically Dr. Baker looked all  
4 together at a total of 160 patients with various  
5 types of wounds. In the first piece it was primarily  
6 diabetic patients with open ulcers and in the second  
7 case it was spinal cord injury and pressure ulcers.  
8 And basically she had a poor group of patient  
9 protocol design where group A received an asymmetric  
10 biphasic model, B received a symmetric biphasic, C  
11 received minimal current, and a control group which  
12 was a sham device. We'll allow you to look at the  
13 results as listed in Appendix A, and basically the  
14 differences in healing rates overall and for her  
15 subgroup analysis were not statistically significant.

16 The other article, and again, remember,  
17 these are just articles that appeared since the  
18 update, is an article by Cosmo, and this looked at  
19 changes in blood flow by laser doppler imaging. And  
20 you will see that several of the articles that are  
21 included here may not have necessarily used wound  
22 healing rate as a primary outcome measure. And  
23 again, this is meant to be as broad as possible and  
24 some of these may be more of a basic science

25 physiology level. Basically they looked at what were  
00175  
1 the changes in blood flow after application of  
2 electrical stimulation. They used low frequency TENS  
3 applied for 60 minutes and basically they then  
4 measured blood flow every five minutes to see how  
5 electrical stimulation was changing blood flow. And  
6 they talk about how their data was statistically  
7 significant at the highest tolerable intensity.

8 It would also be useful to look at some of  
9 the literature reviews and review articles that have  
10 appeared since the ECRI report. There is an article  
11 from the Journal of Food, which you may want to look  
12 at, and Dr. Frantz' article which we spoke about  
13 earlier, the Journal of Geriatric Medicine and again,  
14 these were literature reviews of some of the same  
15 studies (inaudible) as well as some additional  
16 studies also.

17 There's also an unpublished study by Dr.  
18 Frantz which looked at originally 50 patients in that  
19 inclusion criteria, and then eventually there were 37  
20 patients. Again, this is in pressure ulcer Stages II  
21 through IV, and they defined chronic ulcer at least  
22 three months duration. And basically she looked at  
23 number of days for the ulcer to reduce in volume or  
24 surface area by 50 percent from baseline, and she  
25 talks about what her results are there, and

00176  
1 specifically the median time for the volume of the  
2 ulcers in the experimental group reduced by 50  
3 percent, and that was statistically significant.

4 Another article by Dr. Gardner and Dr.  
5 Franz, and this was a meta-analysis, and she talked  
6 about this earlier this morning. I refer you to her  
7 comments this morning. What's important to note is  
8 that she actually did include in her meta-analysis  
9 included chronic wounds that were not just pressure  
10 ulcers but were venous ulcers, arterial ulcers, or  
11 neuropathic ulcers. So there are some studies that  
12 have included arterial ulcers in there study design.

13 There is a clinical trial by Gilchrist  
14 which one of the speakers earlier this morning talked  
15 about. This was the transcutaneous oxygen levels

16 before, during and after application of electrical  
17 stimulation to the foot. Basically it was 132  
18 diabetic patients.

19 There is an article by Jacques, a case  
20 report which was an 81 year old diabetic patient who  
21 received application of device, and Mr. Jacques talks  
22 about what the results were afterwards.

23 There's a review article by Dr. Kloth, and  
24 I think we all know Dr. Kloth's thoughts on the  
25 topic.

00177

1 There is an article by Ms. Ovington, and  
2 several speakers have talked about Ms. Ovington's  
3 article and how she feels that the AHCPR guidelines  
4 should be moved up from level B evidence to level A  
5 evidence, and what she actually bases that  
6 recommendation on is an article by Dr. Wood, which  
7 was just referred to in the previous example.  
8 Basically the Wood article looked at low intensity  
9 pulsed direct current on Stage II through Stage IV  
10 pressure ulcers.

11 And actually at a staff level, we did look  
12 at that article to consider what the basis was for  
13 the discussion about moving from level B to level A,  
14 and we did feel there might be some concerns in the  
15 study design about randomization method, about  
16 inclusion and exclusion criteria, possibility about  
17 the presence of infection, as well as the fact that  
18 not all comorbidities may have been controlled for,  
19 so the patients may not have truly been similar.

20 There's a perspective clinical trial which  
21 again deals with transcutaneous oxygen measures, by  
22 Peter. There's another literature review by  
23 Sheffitt, which appeared in Ostomy Wound Management,  
24 which you have as part of your packet. There is a  
25 case series by Sumano, which appeared in the American

00178

1 Journal of Acupuncture, which talked about 44  
2 patients with various skin lesions and second degree  
3 burns, and basically of those 44 patients, they talk  
4 about 41 patients experiencing an excellent outcome.

5 Just very briefly going through, there's  
6 two articles by Unger which were unpublished studies.

7 One was a randomized double blinded prospective  
8 trial, which randomized 17 patients, nine to an  
9 experimental group, eight to a control group, and  
10 they either received high voltage pulse current or  
11 placebo, and they talk about eight of the nine  
12 experimental patients and three of the eight control  
13 patients experienced complete healing of the wound.  
14 The second trial, which was also by Unger, they had  
15 154 patients, and this is one of those cases where  
16 there were 223 wounds, and they actually did look at  
17 arterial wounds, venous wounds, diabetic, ulcers,  
18 pressure ulcers as well as surgical, and they comment  
19 that of the 232 wounds, 200 wounds healed, 23 were  
20 nonhealed, and the mean healing time was 10.85 weeks.  
21 They didn't provide enough statistical data to  
22 determine whether or not that was statistically  
23 significant.

24 And finally, there was an abstract  
25 published, or actually it was not published, it was

00179

1 an abstract by Zuder, which was a clinical trial  
2 looking at microcirculatory changes as measured by  
3 capillary density, oxygen, pressure and vascular  
4 reserve.

5 So basically, what I wanted to do in that  
6 very quick synopsis is just briefly discuss some of  
7 the additional articles, and there were essentially  
8 11 trials, six case series and five randomized  
9 clinical trials, that appeared since the ECRI report,  
10 and I hope you will take those into consideration as  
11 you continue your deliberations. I hope that's  
12 helpful.

13 DR. GARBER: Thank you very much, John. I  
14 have a question. Did you or any of the other staff  
15 try to pool the results across the better designed  
16 studies, however you might define them, to see if  
17 there were differences in effectiveness according to  
18 the underlying type of ulcer?

19 DR. WHYTE: Certainly that was a  
20 consideration, and I should point out, the reason why  
21 we decided to look at arterial ulcers versus venous  
22 ulcers, versus pressure ulcers, was a discussion with  
23 a wide range of persons that talked about that the

24 healing of ulcers is not the same across the three  
25 groups. And I know there has been controversy over  
00180

1 that, and discussion, and not everyone would agree  
2 with that premise, but we wanted to make sure that  
3 all of you had the opportunity to discuss it and to  
4 look at that, because we could not come to closure on  
5 that. As Dr. Turkelson points out, there is not a  
6 lot of data on arterial and venous ulcers, and so it  
7 was hard to determine.

8 I think one point that I would carefully  
9 consider in the deliberations is the whole issue of  
10 the effect size, and I think you're going to come to  
11 later, and that's something that we have struggled  
12 with in terms of what is essentially the effect size  
13 of this therapy. As many of the speakers have talked  
14 about this morning, it is being viewed as an  
15 adjunctive therapy and where exactly is that role.

16 DR. GARBBER: Les?

17 DR. ZENDLE: I am trying to determine what  
18 added information we get from these studies as  
19 opposed to the studies looked at in the original ECRI  
20 report, and so I'm looking at page 4 of your update,  
21 September 25th, that has the chart, it has the three  
22 types of ulcers across the top and the six types,  
23 modes of therapy.

24 DR. WHYTE: Sure.

25 DR. ZENDLE: I see that Frantz's article  
00181

1 uses TENS in decubitus ulcers and appears to have  
2 some evidence there that was not considered by ECRI.  
3 Do you agree with that, or is this whole methodology  
4 of what I'm trying to do not relevant? I'm trying to  
5 see where there is more information. It looked like  
6 TENS was not addressed in the original set of  
7 articles, but that Frantz's article does address it,  
8 so we could sort of fill in that box.

9 DR. WHYTE: Which Frantz article are you  
10 talking about?

11 DR. ZENDLE: The one that's listed here,  
12 it says unpublished double blind study, 50 patients.

13 DR. WHYTE: Okay, I see that.

14 DR. ZENDLE: Pressure ulcers, medium time

15 to healing, reduction was 50 percent, reduction in  
16 wound surface area.

17 DR. WHYTE: I think that's something that  
18 you have to weigh and take into consideration. What  
19 I would say about the study is, as listed there, that  
20 the data was not statistically significant between  
21 the experimental and the control group at the end of  
22 the study for complete healing as well as median  
23 time, 50 percent reduction in wound surface area. So  
24 I think you have to take that into consideration as  
25 you weigh the information.

00182

1 DR. ZENDLE: What about where it says  
2 median time for volume of ulcer in experimental group  
3 to decrease by 50 percent statistically significant?

4 DR. WHYTE: Right. I think you have to  
5 take all that into consideration, how you weigh that  
6 versus complete healing, versus median time to 50  
7 percent in wound area. All the outcome measures  
8 across studies may not be the same. You have to take  
9 that into consideration as you compare studies, and I  
10 wouldn't necessarily be able to comment in the ECRI  
11 report what their various outcome measures were. The  
12 major outcome measure that Dr. Turkelson described  
13 was about wound healing rate.

14 DR. GARBBER: Any other questions? Okay.  
15 We are at a point now where we have two choices. We  
16 can take a quick break and resume with committee  
17 deliberation or, that would be early for our break,  
18 but we could just go ahead with the open committee  
19 deliberation. What is the sense of the panel?

20 DR. ZENDLE: Go ahead.

21 DR. GARBBER: Go ahead? Anyone who wants  
22 to take a break? If you want to take a break before  
23 our next break, raise your hand.

24 Okay. Now is the time for our open  
25 committee deliberation. I think it would be helpful

00183

1 if everyone grabbed their copy of the questions for  
2 the panel and as you see, again, we have the two  
3 steps about the evidence, is the evidence adequate,  
4 and if we conclude it is adequate, we do need to  
5 assign it to a category of effective size.

6 And now, I would entertain some discussion  
7 about how to proceed. That is, first of all, we can  
8 consider whether we want to lump together the  
9 different types of electrical stimulation or not, and  
10 we can also consider whether we want to deal with  
11 different indications separately. Does anybody want  
12 to start with a suggestion?

13 DR. ZENDLE: I guess the question is also,  
14 how do we discuss the issue of whether this is  
15 primary therapy or only for ulcers that fail  
16 conventional therapy?

17 DR. GARBER: Well, the question as posed  
18 to us is used as adjunctive therapy, which I always  
19 interpret as including primary therapy. And I will  
20 have to ask Sean, if the panel feels they would  
21 rather distinguish between adjunct and primary  
22 therapy, and therapy after other therapies have  
23 failed, if it would be helpful to you if we broke it  
24 up that way, if that's how the panel feels.

25 DR. TUNIS: Yeah, I'm happy for the panel

00184

1 to proceed along, you know, not to mention the  
2 discussion, separating it into primary therapy or to  
3 focus on patients who, I guess it would be the  
4 chronic nonhealing ulcers as an isolated subset, if  
5 that's the feeling from the evidence that's  
6 presented, if that's the way you feel that the  
7 discussions should break out.

8 DR. HOLTGREWE: And then there's another  
9 factor. We have as I understand it, four energy  
10 sources and we have three diseases, so that's 12,  
11 times two is 24.

12 DR. GARBER: Right, and that's one of the  
13 questions. Do we want to proceed by -- let's start  
14 with the energy sources question, because we've heard  
15 a great deal of discussion about the differences and  
16 the amount of evidence there is about differences  
17 between them. Do we want to treat them as a group as  
18 one, basically one set of therapies, or do we want to  
19 distinguish them for the point of view of our  
20 discussions and our final recommendations?

21 DR. OLECK: I would express my opinion,  
22 again, from the questions that I raised and just I



23 have looked at those, I guess we heard some  
24 information here about what the common features may  
25 be of them, and especially with certain subcategories  
00185

1 of the devices. And there seems to have been a lot  
2 of discussion about the high voltage pulse current,  
3 and that was the one that got the favorable rating,  
4 or there was discussion within the AHCPR guidelines,  
5 and a couple of the practitioners here, that's the  
6 one they primarily used, and we kind of talked about  
7 this delivery of charge per second and the  
8 significant things there.

9 And yet, with some of the other  
10 modalities, just the straight direct current, the  
11 nonpulsed direct current, and the pulse  
12 electromagnetic items, I think we've heard much less  
13 information about those, and I'm uncomfortable just  
14 from a clinical standpoint without better  
15 understanding and without better evidence of those,  
16 of just lumping everything together and saying that  
17 this works or this doesn't work. That any type of  
18 electrical device, if we are looking at these  
19 particular devices, and as we get that information or  
20 this information is given to HCFA, does this then  
21 apply to every conceivable device that someone has  
22 that would plug into an electrical outlet or hook up  
23 to a battery and you know, could that conceivably  
24 used, would this recommendation apply to that or does  
25 it only apply to certain categories of devices?

00186

1 DR. GARBER: Could I just ask you to turn  
2 that into language we could use, or could I take a  
3 stab at something?

4 DR. ZENDLE: I think that's the point, we  
5 can't.

6 DR. GARBER: Well, no. Let me just -- I  
7 hate as the chair to propose language, and I'm not  
8 proposing this except to find out if this is what the  
9 panel would feel comfortable with, and that is that  
10 we state that our discussion concerns the forms of  
11 electrical stimulation that have been tested in the  
12 literature, and we have concluded that there is not  
13 enough evidence to determine whether or not the

14 different forms of electrical stimulation differ in  
15 effectiveness. That is not a conclusion about  
16 whether or not it should be covered, by the way.  
17 This is just about whether we lump them together or  
18 not. Is that the sense of the panel or should it be  
19 something different? Mike?

20 DR. MAVES: That's at least where I think  
21 I'm at this point, Alan. And in fact, looking at the  
22 questions that HCFA posed, I sort of perhaps  
23 incorrectly assumed that this would be a group  
24 decision from the beginning. But I think you have  
25 captured this. I just don't think there is enough

00187  
1 there for us to say one form is better or worse than  
2 the others, so I would go along.

3 DR. GARBER: And Les?

4 DR. ZENDLE: I just have a question. And  
5 that's, what's to prevent somebody from putting a  
6 black box with a plug in it and saying it is one of  
7 these six things? Doesn't the FDA have to say it's  
8 doing what it says it does? Do we really need to be  
9 the ones that say that these different things are all  
10 efficacious?

11 DR. GARBER: Well, I think a body like  
12 this cannot get into great detail about differences  
13 between devices or any other treatment where there  
14 are minor differences. So I mean, if we were to  
15 conclude that this broad set performs electrical  
16 stimulation, had enough evidence it was effective, it  
17 would be HCFA's job to decide if something new fit  
18 into this category. It's kind of like getting a,  
19 what you call it, clearance. Yes, Bruce.

20 DR. SIGSBEE: Every device manufacturer  
21 has to run it by the FDA to get approval, and they  
22 cannot use it on patients until it's been very  
23 thoroughly studied, so I don't think that that's  
24 really our issue.

25 DR. GARBER: So, are there any objections

00188  
1 to proceeding on this basis, that we're lumping  
2 together, and I guess they were agnostic about  
3 whether or not there are any differences in the  
4 effectiveness. Yes, Angus?

5 DR. MCBRYDE: Not just the device, but if  
6 you look through all these things, I mean, we're  
7 talking once or twice a day, two up to seven times a  
8 week, are we talking half an hour duration or ten  
9 minutes duration, as well as wave form, charge, the  
10 actual hardware itself, so I think all that has got  
11 to be lumped, and leave that as a quality control  
12 type matter.

13 Second, a large item that just kind of  
14 bothers me is well, let's get rid of this, and then  
15 we'll talk about primary versus adjunctive.

16 DR. GARBER: Yes, Mike.

17 DR. MAVES: Alan, if I could just suggest  
18 one thing, I think that -- and this is sort of  
19 separate from any discussion regarding where we're  
20 going to go with this, but I think the discussion we  
21 had about the dose response, the frequency, type, all  
22 are questions, if you will, that would be very good  
23 to send back to HCFA and to say, these are the kinds  
24 of things I think that ought to be encouraged in  
25 future studies. Because I think all of us felt a

00189

1 little ambiguous about that, and this is sort of  
2 separate from that. I mean, I don't want this to  
3 prejudice in any way our discussions, but I had noted  
4 down that I thought all of those would be primaries  
5 for research, and for HCFA to make that  
6 recommendation back to the manufacturer.

7 DR. GARBER: All right. Incidentally,  
8 taking that suggestion, there's nothing to stop us as  
9 a panel from putting that into our final conclusions,  
10 that is, there are certain areas where we think  
11 further research might be helpful, areas of  
12 uncertainty that could potentially be addressed with  
13 further study.

14 DR. HOLTGREWE: Well, you know, I am  
15 struck in the area of cancer for instance, in  
16 chemotherapy and surgery, you have certain  
17 parameters. A dose of cisplatin is reasonably  
18 established somewhere along the line. And in the  
19 area of surgery, certain surgical techniques, the  
20 inclusion of the adrenalectomy with radical  
21 nephrectomy is included in the literature, and I'm

22 just struck here that the literature is terribly weak  
23 in the area of how long is the machine on, which  
24 machine do you use, and it's a total mixed bag. It's  
25 just succotash rather than science at this point.

00190

1 DR. GARBER: Bruce?

2 DR. SIGSBEE: I just wanted to make a  
3 brief comment about technique. There are two fairly  
4 large articles that have come out since the ECRI  
5 report, both by Baker, and they used a nonstandard  
6 technique where they had electrodes that were distal  
7 and proximal to the ulcer, and that's quite different  
8 from a technique where the ulcer, either the cathode  
9 or anode is on wet gauze within the ulcer bed itself.  
10 So it may be at least from a technical standpoint,  
11 that that seems to be a technique that should not be  
12 employed.

13 DR. ZENDLE: Not? I'm sorry, the last  
14 phrase you said there, Bruce?

15 DR. SIGSBEE: That that's a technique that  
16 should not be employed. They seem to be well  
17 designed studies with good end points and with large  
18 numbers of patients, and they did not reach  
19 statistical significance where they used something  
20 quite different from the other techniques that have  
21 been described here.

22 DR. GARBER: Okay. Mike?

23 DR. MAVES: I was just going to make the  
24 comment, while I think those are important areas to  
25 look at, you're dealing with a biological system, and

00191

1 for instance, as an EENT doctor we fit individuals  
2 with hearing aids, and there is a broad parameter  
3 over how much amplification you can give someone, but  
4 for each individual patient there is a specificity  
5 that's determined by their level of hearing loss,  
6 their comfortable level. So, while I'd like to see  
7 this improved, I think one, you also have to  
8 understand you're dealing with a system here where  
9 probably inherently, this may be as good as you're  
10 going to be able to quantify some of these  
11 parameters, at least at this point in time.

12 DR. GARBER: Were there any other hands up

13 down there? I can't see that well at that end of the  
14 table. Les?

15 DR. ZENDLE: I'm sort of thinking out loud  
16 here, which I know is dangerous, but the idea that  
17 studies, some of them are primary, some of them are  
18 secondary, some of them had people who failed  
19 conventional therapy cross over for the electrical  
20 stimulation and then did better, but some of them  
21 didn't have that model. Can we sort of say we're not  
22 going to address that either, that whether or not  
23 this is -- or do we want to go on record as saying  
24 that we have an opinion about primary-secondary  
25 treatment, or primary but not secondary treatment, or

00192

1 something like that? I would be interested in  
2 hearing what the rest of the panel has to say about  
3 that too.

4 DR. GARBUR: That definitely could be  
5 something the panel could come to a decision about,  
6 do we split off the group that failed primary therapy  
7 and so therefore, deal with two different situations?

8 DR. ZENDLE: And I mean, the other thing  
9 I'm asking is, would HCFA find it totally unuseful if  
10 we said we're not going to split out anything because  
11 the literature doesn't allow us to do that, we're  
12 going to lump everything together and say that there  
13 appears to be evidence supporting the efficacy in  
14 some patients but the studies don't allow us to  
15 distinguish which patients it is.

16 DR. TUNIS: I just want to try to also  
17 tease apart, because I think this notion of primary  
18 versus secondary therapy, because I might be two  
19 differential notions there. One is, you know,  
20 looking at the issue of treating patients with  
21 chronic nonhealing ulcers as opposed to, you know,  
22 acute ulcers, in other words, by some definition,  
23 there is some objective definition that an ulcer is  
24 nonhealing. So that's a separate issue from whether  
25 you're looking at patients, all of whom are chronic

00193

1 nonhealing ulcers, you know, try a therapy and then  
2 for those who fail even that, switch them over. It  
3 seems like those are two somewhat distinct issues.

4 DR. ZENDLE: When I say it is nonhealing,  
5 it means it has not responded to conventional  
6 therapy.

7 DR. TUNIS: Right. It's just that there  
8 are different courses in the process of a wound  
9 before it even gets to the point where it's a  
10 nonhealing wound, so go ahead.

11 DR. GARBER: Bruce.

12 DR. SIGSBEE: The problem is that anybody  
13 looking at this may choose to use as their study  
14 population the folks who have failed conventional  
15 treatment, and you know, obviously I am most familiar  
16 with anticonvulsants, and that's where you use the  
17 new anticonvulsants, for those who are uncontrolled  
18 on standard treatment. And yeah, it's generalized to  
19 treatment of all seizures and those medications are  
20 assumed to treat. And the question that I think we  
21 probably ought to spend some time on is, the bulk of  
22 the evidence we have in front of us is on patients  
23 who failed conventional treatment. Is there  
24 sufficient evidence here to warrant expansion of this  
25 to the treatment of decubiti and other chronic

00194  
1 ulcers, or should we recommend that it be restricted  
2 to those who have failed conventional treatment,  
3 however that's defined.

4 DR. GARBER: Logan, and then Angus.

5 DR. HOLTGREWE: I think Les has summed it  
6 up very well. I think the level of evidence, such  
7 that we have here, is such that it's very difficult  
8 if not in fact impossible to break it out into the  
9 three different kinds of ulcers and the four  
10 different kinds of clinical energy. I think there is  
11 evidence to show that there is some merit to this  
12 based on pure clinical grounds. The pathophysiology  
13 is obscure, the exact dosages are obscure, and I  
14 think to go beyond that, I think is impossible. I  
15 personally would be terribly uncomfortable trying to  
16 find a certain energy type for a certain treatment  
17 for a certain ulcer, I mean, we don't have that. I  
18 think all we can say is there seems to be some  
19 efficacious advantage to using this therapy, and  
20 stop.

21 DR. GARBER: Angus?

22 DR. McBRYDE: Well, it seems like we have  
23 jumped from the logistics of application to primary  
24 and secondary. What bothers me as an orthopedist is,  
25 and of course we've got our own problems with the

00195

1 bone stimulator, is that there at least are accepted  
2 parameters for delayed union, nonunion, and so forth.  
3 But even though you say a recalcitrant ulcer or a  
4 primary ulcer, there's a huge gray zone in the  
5 middle. So that is another piece of the definition  
6 that's got to be done in a big way before you can  
7 even say what we mean between primary and  
8 recalcitrant.

9 DR. SIGSBEE: That's a job for staff.

10 (Laughter.)

11 DR. GARBER: Just to take us on to the  
12 next step, I think we're agreed we are not going to  
13 separate out the types of machines at all. But now  
14 the question we face is do we want to separate out,  
15 can we give a good definition of the clinical  
16 situation, i.e., failed conventional therapy and we  
17 have to define what we mean by fail and what we mean  
18 by conventional therapy. But if we have decided, we  
19 could just start there and ask if there is adequate  
20 evidence in that situation, or we could just say for  
21 any lumped together, all different cases, which would  
22 include so-called primary therapy, that is chronic  
23 but hasn't undergone and failed all conventional  
24 therapies. So, which of those two routes would you  
25 like to go, or would somebody want to propose another

00196

1 one, i.e., only discuss after having failed primary  
2 therapy, or just lump it together? Les?

3 DR. ZENDLE: I think as far as evidence,  
4 you can't say that it -- the only evidence presented  
5 consistently is for failed therapy, conventional  
6 therapy, so I would, I think we should address  
7 whether we can accept it for patients who have failed  
8 conventional therapy, then talk about whether we want  
9 to try to separate the three types of ulcers for  
10 people who failed conventional therapy. And I will  
11 just tell you that I also don't think we can do that.

12 But then we can address, what about people  
13 who have not failed conventional therapy, and I would  
14 say there is no evidence no support its use in that  
15 situation.

16 DR. GARBER: Well, I would just like to  
17 take this step-wise, so first let's address that  
18 first part. Should we separate failed conventional  
19 therapy? Mike?

20 DR. MAVES: Again, I think perhaps this is  
21 just sort of the bias of reviewing these things at  
22 home, but my sense was that we were dealing with sort  
23 of chronic nonhealing ulcers of a variety of types  
24 that I guess by definition were not acute and  
25 perhaps, more probably I guess that was maybe my

00197

1 assumption, it had some form of prior therapy, but  
2 presented real kind of therapeutic dilemmas. And the  
3 few cases that we saw here were certainly suggestive  
4 of that. So I guess from my standpoint, I assumed we  
5 were dealing essentially with a clinical entity  
6 called chronic nonhealing ulcers of a variety of  
7 etiology, and I did not at least in my mind going  
8 through these, consider there to be a difference  
9 between an acute and chronic situation.

10 DR. ZENDLE: Anybody disagree?

11 DR. GARBER: I'm trying to figure out what  
12 that means.

13 DR. MAVES: I would lump them together.

14 DR. GARBER: Okay. So you would not  
15 distinguish. Well, your --

16 DR. ZENDLE: He would lump the nonhealing  
17 ones together.

18 DR. MAVES: Yes.

19 DR. GARBER: Yeah. I think this comes  
20 down to precision of definition, what you mean by  
21 chronic nonhealing. And I guess this should be  
22 driven in part by what you need in terms of language  
23 for coverage, what is interpretable in a coverage  
24 context.

25 DR. TUNIS: Yeah. I can also ask some of

00198

1 the analysts that worked on this, if it's not out of  
2 order, and I would even ask some of the folks who



3 have come to testify whether there are objective  
4 definitions that are usable for chronic nonhealing  
5 ulcers, and maybe we can get some thoughts on that.

6 DR. GARBER: Yeah. Charlie?

7 DR. TURKELSON: Our report focused on  
8 ulcers that have been present greater than 30 days.

9 DR. GARBER: Regardless of what treatments  
10 were given?

11 DR. TURKELSON: That's right.

12 MS. UNGER: Just a couple comments. I  
13 suggest that you look at the Wound Healing Society  
14 definition of a chronic wound and use our  
15 conventional wound community distinctions between  
16 acute and chronic, and then you know, we're moving in  
17 the face of a lack of evidence based to large dialogs  
18 about best practices. And so instead of maybe  
19 talking about conventional therapies, the issue might  
20 be using an adjunctive therapy when best practices  
21 have not resulted in healing, and that may then mean  
22 something in the wound healing community where  
23 there's a body of literature emerging on best  
24 practices.

25 DR. GARBER: You know, I would actually

00199

1 like to suggest picking up on a suggestion that  
2 somebody else made. If the panel agrees, this is  
3 something that we could let HCFA and HCFA staff work  
4 out, in consultation with the relevant professional  
5 societies, because I think above all, we want  
6 whatever recommendations we make to be readily  
7 interpretable by you and by the clinical community  
8 who will have to deal with it. I'm not sure we can  
9 get to that level this afternoon, but I think we  
10 would trust you in consultation to define that a  
11 little better.

12 DR. SIGSBEE: I want to be a little bit of  
13 a devil's advocate here, and a decubitus is a  
14 decubitus, and maybe you have one that's chronic  
15 nonhealing, and is the underlying healing process  
16 different from that compared to one that perhaps  
17 hasn't been given a strong course of conventional  
18 therapy? And at least reviewing all these articles,  
19 there is some evidence that the rate of healing is

20 faster using electrical stimulation, and maybe there  
21 is an argument to be made, and this may be an  
22 analysis that HCFA staff has to go through, the cost  
23 effectiveness of dealing with this on an earlier  
24 basis rather than ending up with a chronic ulcer that  
25 delays going home, all those other kinds of issues.

00200

1 So I'm not sure that apriori we should restrict our  
2 comments purely to just the chronic nonhealing  
3 ulcers, even though the evidence before us deals with  
4 that issue.

5 DR. GARBER: Well, let me suggest that we  
6 vote on chronic nonhealing ulcers first and after  
7 that, we can decide whether we want to extend beyond  
8 that. So, I think we have this resolved. Does  
9 everybody agree with this proposal, the exact  
10 definition of chronic nonhealing can be worked out by  
11 HCFA? And so I think we all have a general sense of  
12 what that means even if we can't be precise about it.

13 Then the next question, Les has suggested  
14 we lump together pressure ulcers along with the other  
15 types. And the alternative is to distinguish  
16 pressure, maybe venous, and arterial and neuropathic,  
17 or something like that. What is the sense of the  
18 panel about lumping versus splitting on the clinical  
19 condition?

20 DR. HOLTGREWE: Lump.

21 DR. SIGSBEE: Maybe we could phrase it  
22 that at present, the quality of evidence before us  
23 did not allow us to distinguish.

24 DR. ZENDLE: That's why we lump.

25 DR. GARBER: Well, one way to put this, is

00201

1 do people have concerns that there is -- is there  
2 sufficient evidence to be concerned that there really  
3 may be differences in effectiveness across these  
4 clinical types?

5 DR. ZENDLE: One of the things, and I  
6 think it gets back to your last point, I have less  
7 concern about lumping if we restrict it to chronic  
8 nonhealing ulcers.

9 DR. GARBER: Okay. Any disagreement? We  
10 haven't had a real vote yet, but we're actually only

11 discussing procedural issues at this point. So the  
12 way things stand now, our first question will be, is  
13 there adequate evidence to draw conclusions about  
14 effectiveness of electrical stimulation as an  
15 adjunctive therapy for chronic nonhealing pressure  
16 ulcers? And we are not going to distinguish the  
17 ulcer types or the types of --

18 DR. ZENDLE: Take the word pressure out.

19 DR. GARBER: Pressure, I'm sorry, yeah.  
20 Chronic nonhealing ulcers. Thank you for that  
21 correction.

22 Okay. Now I will entertain a motion.

23 DR. TUNIS: Before you do that --

24 MS. CONRAD: Let me read this into the  
25 record first. For today's panel meeting, voting

00202

1 members present are: Michael Maves, Kenneth Brin,  
2 Logan Holtgrewe, Angus McBryde, Bruce Sigsbee, and  
3 Les Zendle. A quorum is present, and no one has been  
4 recused because of conflicts of interest. Thank you.

5 DR. GARBER: Go ahead.

6 MS. UNGER: Just a clarification that the  
7 group of wounds that are of interest here are not  
8 just ulcers, and the largest groups are probably  
9 diabetic, venous, then pressure is the smallest large  
10 group; and then the subgroups being arterial --  
11 nonhealing surgical wounds is certainly a large  
12 potential group of patients, so perhaps using the  
13 word wounds instead of ulcers would be more  
14 appropriate.

15 DR. ZENDLE: I am comfortable with that.

16 DR. SIGSBEE: But the thing is that we've  
17 had absolutely no evidence presented to us that dealt  
18 with nonhealing surgical wounds, and at least I don't  
19 have any personal knowledge and we haven't had any  
20 presented, presentations from the discussions, about  
21 whether that pathogen and the treatment has parallels  
22 or nonparallels, and I would have a very hard time in  
23 any way commenting on whether that's an appropriate  
24 step or not. We've really dealt with the ulcers that  
25 we have been provided with initially.

00203

1 DR. GARBER: So you would reject the

2 change in language and leave it ulcers?

3 DR. SIGSBEE: Right.

4 DR. GARBER: Is that the sense of the  
5 panel?

6 DR. ZENDLE: I have a semantic question.  
7 It does refer to, it says specific types of wounds,  
8 and then it says decubitus ulcers, venous ulcers,  
9 diabetic ulcers, and that indeed is what the  
10 literature was that we reviewed. I think if we  
11 define it as that, and we can use the word wounds,  
12 and then say we are referring to these three types of  
13 ulcers.

14 DR. GARBER: Okay, the panel is in  
15 agreement? Marshall?

16 DR. STANTON: Well, just maybe if Sean  
17 could clarify, that might reassure some people in the  
18 audience, that just because the panel doesn't address  
19 something doesn't mean that HCFA in its coverage  
20 language of E-stim is limited to just what the panel  
21 has addressed. HCFA is able to still make coverage  
22 decisions without the input of the panel on things  
23 that we did not address in E-stim.

24 DR. TUNIS: Right. And obviously to the  
25 extent that the panel either briefly or at any length  
00204

1 wants to discuss, you know, the issue of ulcers  
2 outside of these three, or wounds beyond the three  
3 that we discussed here or for that matter, wounds  
4 other than the chronic nonhealing wounds, any  
5 discussion the panel wants to have about that, we  
6 would certainly take into account. But you're right,  
7 just because the panel decides not to discuss it,  
8 doesn't mean that we wouldn't address it in the  
9 coverage policy.

10 DR. HOLTGREWE: Yeah, but our comments  
11 here have to be totally restricted to these three  
12 types of ulcers, because that is all we have  
13 reviewed, we reviewed nothing else, and to go beyond  
14 that would be inappropriate.

15 DR. GARBER: And also Bruce has just  
16 pointed out, it also includes arterial ulcers. I  
17 mean, there's some question about how much data there  
18 is about arterial ulcers.

19 DR. HOLTGREWE: Well, that's true.  
20 DR. ZENDLE: I thought arterial and  
21 diabetic are synonymous, no?  
22 DR. HOLTGREWE: Well, I thought so.  
23 DR. STANTON: The diabetic could be  
24 arterial plus minus neuropathic, and you could have  
25 some arterial that are pure arterial, but there's not  
00205  
1 much evidence for anything.  
2 DR. GARBER: Now, I think we are pretty  
3 much in agreement on this, so I'll entertain a motion  
4 about the first question.  
5 DR. ZENDLE: So moved.  
6 DR. GARBER: The motion is therefore, I  
7 assume, to accept, to answer yes to the first  
8 question as amended, which now says chronic  
9 nonhealing ulcers, that the evidence is adequate.  
10 The motion is to answer yes. Is there a second to  
11 the motion?  
12 DR. BRIN: Second.  
13 DR. GARBER: Okay. Discussion?  
14 DR. ZENDLE: Is there something specified  
15 that we also, when we refer to electrical  
16 stimulation, we're not distinguishing between the  
17 different types?  
18 DR. GARBER: That's in the transcript.  
19 DR. ZENDLE: Okay.  
20 DR. GARBER: Mike?  
21 DR. MAVES: The only other thing was the  
22 little note on the semantics as to how we were going  
23 to refer to those, I think that's important to have  
24 in the language of the resolution. Someone had that  
25 somewhere, and I didn't get a chance to jot that  
00206  
1 down. It was sort of chronic nonhealing ulcers, but  
2 then as sort of a paren, I think we had chronic  
3 nonhealing wounds --  
4 DR. SIGSBEE: And then parentheses, the  
5 four types of ulcers we've talked about.  
6 DR. MAVES: Is that the language that we  
7 want to include?  
8 DR. GARBER: I will make an attempt. Is  
9 the evidence adequate to draw conclusions about the

10 effectiveness of electrical stimulation as an  
11 adjunctive therapy for chronic nonhealing wounds  
12 (pressure ulcers, venous ulcers,  
13 arterial/neuropathic)? That's it. The motion on the  
14 floor is to answer that question in the affirmative.

15 DR. STANTON: Is it possible then for you  
16 to vote on that question before having a discussion  
17 about what people feel about the level of evidence  
18 that's there before deciding that it ought to be  
19 lumped together? Does that mean that people have  
20 decided for themselves that the level of evidence is  
21 either there for all of those or not there for all of  
22 those, and that's why they're comfortable lumping  
23 them together?

24 DR. GARBER: That's what we meant by  
25 having that discussion about procedures, that people

00207

1 felt they would like to proceed to answer the  
2 question about the evidence in the aggregate about  
3 the different types of machines and the different  
4 clinical indications. Now at this point it would be  
5 appropriate for you to discuss, if you think you  
6 can't answer yes, because you think the evidence is  
7 greatly different from one indication to another and  
8 you'd say yes to one but not another, we should have  
9 actually had that discussion before and not split, if  
10 you feel that way. But if you are uncomfortable with  
11 it, you should bring it up now before it's really too  
12 late.

13 DR. STANTON: Well, it seemed like we had  
14 some discussion on the question of the different  
15 pulses and how to deliver them, and people seemed to  
16 agree that there wasn't a good way to split it, and  
17 so everybody seemed agreeable about lumping. I  
18 didn't see that same discussion for the three or four  
19 different types of ulcers there are, and I guess my  
20 own sense is that I felt there was a difference in  
21 the body of literature as best I could split them  
22 apart for the different ones, and I just would like  
23 to hear some other people's opinions. It seems like  
24 we went very quickly to the point of lumping it  
25 together and I didn't really hear much opinion, I

00208

1 just heard people kind of say yeah, lump it.

2 DR. GARBBER: Les?

3 DR. ZENDLE: I think there may be a  
4 difference in the literature between the different  
5 kinds of ulcers, but by limiting it to chronic  
6 nonhealing ulcers, which in my mind by definition,  
7 they tried other stuff and it hasn't worked, it seems  
8 to me appropriate to use electrical stimulation. And  
9 that's why if we lump them all together, I can vote  
10 yes on electrical stimulation. If you start dividing  
11 them up, I don't know how I'm going to vote on each  
12 of those things, because I don't think there's enough  
13 evidence to allow us to say this is and this isn't,  
14 unless we limit it to the broad category.

15 DR. STANTON: What I wonder about and  
16 don't know for sure is whether some people would  
17 think the exact opposite, that by lumping it  
18 together, it makes the body of evidence less clear  
19 and makes some people perhaps less comfortable, where  
20 they may have been more comfortable in one area and  
21 not others. Now I don't know one way or the other, I  
22 would just like to hear a little more discussion on  
23 it.

24 DR. GARBBER: Mike, and then Bruce.

25 DR. MAVES: I concur with that same

00209

1 opinion. I think the fact that it is chronic  
2 nonhealing, makes me much more comfortable about  
3 putting the three together and being able to answer  
4 in the affirmative on that. And so, had that not  
5 been the case, you know, I think there are at least  
6 from what we've seen, perhaps some differences, but  
7 it may well be due to simply case accumulation and  
8 numbers, more of a problem rather than simply not  
9 adequate studies. So I think when it's chronic  
10 nonhealing, there has been some therapy tried  
11 beforehand, I think that actually makes the  
12 distinction between the three of these, which may be  
13 a matter of semantics when you're actually on the  
14 ground, much easier.

15 DR. SIGSBEE: You now, I think if you look  
16 at it, there is in fact different levels of evidence  
17 based on the ulcer type, but I think it's based n

whether they have been studied or not. The pressure ulcers have had a large majority of the studies. There was one study that happened to use alternating current in venous stasis ulcers, but it hadn't really been looked at critically in pressure ulcers, and the others hadn't been studied in the same critical fashion, so I think it's a matter of what patient population we looked at. At least

00210  
1 pathophysiologically I don't see that there's  
2 compelling evidence that there is a basic difference  
3 in these chronic nonhealing ulcers and I would be  
4 more comfortable dealing with them as an aggregate  
5 rather than separating them out without clear  
6 evidence that they should be separated out.

7 DR. GARBBER: At the risk of restating the  
8 obvious, just to build on what Bruce just said, you  
9 don't have to feel that the levels of evidence are  
10 equal for all of these areas in order to conclude  
11 that the evidence is adequate overall. And  
12 inevitably when we're in a situation where you could  
13 split things and want things, you're going to have  
14 differences in the level of evidence. That's why we  
15 have a hard time making a decision. But you  
16 certainly could feel that the evidence is much  
17 stronger in one area than another, yet conclude that  
18 overall the evidence is adequate. And if you felt,  
19 though, that there was too large of a discrepancy,  
20 then you should clearly not lump them, that is, where  
21 you thought there was really no evidence whatsoever  
22 for indication three, then we should probably split  
23 it off if there's that great a discrepancy. But I  
24 had concluded that implicit in the panel's feeling  
25 that they should lump these together was that the

00211  
1 differences in levels of evidence were not so great  
2 as to make it necessary to consider each of these  
3 indications separately. Dr. Oleck?

4 DR. OLECK: One of the things that wasn't  
5 focused in a lot is in terms of safety, and I think  
6 overall the safety of these, you know, seems to be  
7 very good. I guess when you raise the issue about  
8 arterial ulcers, and there was some discussion about



9 you know, when you give too much, and could there be  
10 some damage. Are people with arterial ulcers more  
11 susceptible to giving too much or inappropriate  
12 amounts of electrical stimulation, and does that make  
13 those people, you know, a little more questionable?  
14 I don't know. We really haven't heard very much  
15 information about that, but this is just a concern  
16 that I have listening to what testimony you have had  
17 here.

18 DR. TUNIS: Can I just make one kind of a  
19 comment just on the sort of the preferences expressed  
20 on the particular issue that you're talking about,  
21 splitting down and having individual voting and  
22 discussion. The preference would be that the panel  
23 try to do that. You know, going to whether it's  
24 feasible to do that given the data that's presented,  
25 but it's also possible procedurally to try to do it

00212

1 one at a time for the different types of ulcers, and  
2 then come back and try to do it as an aggregate or  
3 some variation of that. But at least I would just  
4 like to pose as, if the panel feels it's feasible,  
5 that we try to do it split rather than lumped.

6 DR. ZENDLE: My concern is that if you  
7 break it up, I feel that I am on much shakier ground  
8 making any kind of decision. And by lumping it, it  
9 allows me to feel semi-okay about reaching a  
10 conclusion. By splitting it out, I don't feel I  
11 could reach a conclusion.

12 DR. TUNIS: Okay.

13 DR. ZENDLE: Except for the decubitus.

14 DR. TUNIS: I translate that to saying  
15 that on each of the sort of four questions about the  
16 adequacy of evidence, if you separate it out by type  
17 of ulcer, you simply wouldn't be able to answer that,  
18 so let's just go ahead and try to answer it as an  
19 aggregate; is that right?

20 DR. ZENDLE: I would probably abstain on  
21 everything but decubitus ulcer.

22 DR. MAVES: And I would concur, Sean. I  
23 think it's a situation where I think it may be a  
24 problem, and I understand from your standpoint it may  
25 be, but you're asking us to look at this evidence and

00213

1     come up with our best call. Given the question that  
2     HCFA has come up with that makes it a touch  
3     uncomfortable for you, I think for us, it makes the  
4     decision, at least in my mind, much easier to have  
5     these all together at this point, signifying that,  
6     though, when you design your payment policy.

7             DR. GARBER: Sean, if I could just  
8     recapitulate parts of the earlier discussion about  
9     lumping or splitting, Les and others said that they  
10    felt more comfortable because this was restricted to  
11    chronic nonhealing, meaning that it had failed some  
12    form of good therapy for a long enough time. And as  
13    they interpret the evidence, you could draw a  
14    conclusion about that, and also perhaps they could  
15    draw a conclusion if we split it the way HCFA asks  
16    the questions, they could comfortably draw a  
17    conclusion about pressure ulcers, and they have more  
18    doubts about the other kinds of ulcers, but they  
19    didn't feel that was useful. Is that a fair  
20    restatement?

21            So I think you're hearing the panel trying  
22    to be responsive to your needs, but they're saying  
23    that the scientific evidence stacks up, the totality  
24    of evidence stacks up this way and doesn't lend  
25    itself easily to the breakdown that you proposed.

00214

1             DR. TUNIS: Yeah, and I'm not feeling  
2     strongly, like imposing any counterintuitive or  
3     counteranswerable framework on the panel, but I just  
4     want to make sure that I do understand the point that  
5     was just made, I think it was by Les, that sort of  
6     restating what you just said, that basically you're  
7     saying if you are asked to split this up and vote on  
8     the four separate ulcer types, you would have to  
9     abstain on everything except pressure ulcers; is that  
10    right?

11            DR. ZENDLE: Well, I think you have to  
12    combine it with what Alan just said too, that it also  
13    pushes the question for the chronic nonhealing and so  
14    I think I misspoke before.

15            DR. TUNIS: So you would more defer to  
16    Alan's formulation of it, the way Alan sort of

expressed the need to try to respond to the question in aggregate as opposed to individually.

DR. ZENDLE: I don't think we have enough information to split out the chronic nonhealing ulcers. We don't have enough information to split out the different kinds, and I'm comfortable voting yes on the lumping because it's chronic nonhealing. Does that make sense?

DR. TUNIS: Yes, that makes sense.

00215

DR. GARBER: Bruce?

DR. SIGSBEE: Just to elaborate a little bit more, there are pieces of studies that have been done on these different populations. Alternating current was done on venous stasis. Some of the stuff in Appendix A looks at blood flow changes in diabetic neuropathic ulcers and shows that there is an increase in blood flow with electrical stimulation. So there are different pieces that have been offered and I think in aggregate, I think it's a pretty compelling group of evidence. If you start dissecting it into subgroups, it becomes less compelling for each of the subgroups, and I think at least for me, it's harder to make a decision about the weight of the evidence and try to advise HCFA on where this is from a clinical medical standpoint.

DR. TUNIS: Well, why don't we proceed? I'm also getting mindful that we are maybe at this point overdue for a break, so maybe you don't want to do that in the middle of a motion.

DR. GARBER: Well, we do have a motion on the table, and we've discussed it. Do people feel ready for a vote? Okay. Do I need to reread the motion? I'll take that as a clear no. All in favor of the motion, raise your hands.

00216

MS. CONRAD: Unanimous, okay.

DR. GARBER: Now, shall we take a break?

DR. TUNIS: Sure.

DR. GARBER: Okay, 15-minute break please.  
(Recess.)

DR. GARBER: Okay, if we could, I would like to beg the indulgence of the panel members. We

8 had a very helpful discussion and we reached a vote,  
9 and I'm left in kind of a quandary because when I  
10 report to the Executive Committee and I know this is  
11 also something Sean needs, I have to report about the  
12 reasons for the decision and so on, and I think I can  
13 do that. But I also need to get the sense of the  
14 panel about the original three clinical indications,  
15 i.e., the pressure ulcers, or four, however you want  
16 to describe it.

17 And I want to make sure, and I would like  
18 a vote on this, because I want to be accurate. I  
19 stated before that I thought the sense of the panel  
20 was that there was strong evidence for pressure  
21 ulcers and that the evidence was substantially weaker  
22 for the other indications. So first of all, I would  
23 like to get a sense of the panel with the vote, is  
24 the evidence adequate for pressure ulcers? Again,  
25 this is for all of the treatment modalities combined?

00217

1 So if you could us just raise your hand, is the  
2 evidence adequate for pressure ulcers taken alone?

3 DR. STANTON: Now, wait a second. Are you  
4 voting?

5 DR. GARBBER: This is not -- we are going  
6 to proceed along our vote from before. We still have  
7 to report something about these indication, or I have  
8 to. What we are proceeding, the step two is going to  
9 be rating the magnitude of the effect as we had voted  
10 before, that is, for chronic nonhealing ulcers, we  
11 are not changing any of that. But I am going to have  
12 to -- I mean, you could just whisper in my ear, that  
13 wouldn't be appropriate, about what you think, but I  
14 have to report about the clinical indications.

15 DR. STANTON: Well really, from a  
16 procedure standpoint, I guess I feel a little  
17 discomfort with that, because either you vote along  
18 what you want to go to the Executive Committee, or  
19 you decide for whatever reason there is a better way  
20 to vote, and you vote that way, and that's what it  
21 seemed like what you were doing. And I don't have a  
22 strong -- I don't care either way, but I think that  
23 from a process standpoint, you want to have a vote on  
24 the message that is sent. I don't think that there

25 should be an unofficial vote that is going to be the  
00218 message.

1 message.  
2 DR. GARBER: Well, this is -- go ahead,  
3 Les.

4 DR. ZENDLE: I think most of us could  
5 agree that the evidence is best for pressure ulcers.  
6 What I'm uncomfortable with, and maybe others are  
7 too, is at what point does a yes go to a no, and I'm  
8 not sure where that line is. And that's why I'd  
9 rather -- I'm not -- that's why I'm not sure that  
10 what you're proposing is that helpful to anybody.

11 DR. GARBER: Actually, Les, let me clarify  
12 one thing, though. I'm not saying to vote up and  
13 down every indication, but I want to know if I'm  
14 accurate in saying that the panel felt, and this was  
15 my sense from the discussion, and I could just go and  
16 say this without you voting or telling me --

17 DR. ZENDLE: So you're just asking for one  
18 sort of straw poll.

19 DR. GARBER: Is the evidence much stronger  
20 for pressure ulcers than for the other indications?

21 DR. ZENDLE: Oh, I thought you were going  
22 to ask us to vote on the other two.

23 DR. GARBER: Well, we could do it that way  
24 but no, I don't want to give the appearance that  
25 we're going to renege on a decision we made, first of

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1 all. And secondly, when we proceed to question two,  
2 that is about the size of the effect, it has to be  
3 along the lines that we already voted, that is,  
4 divided up and defined the way that we actually did  
5 define it. So let me be clear. Marshall, I can  
6 appreciate your concerns, but I want to make it clear  
7 that we are not talking about revisiting the issue in  
8 a different forum.

9 But certainly when I explain this, and  
10 this is what happened at the last Executive Committee  
11 meeting, I had to give the panel's reasons and why  
12 they went one way and not the other. I am perfectly  
13 happy to just give my opinion again, but if there  
14 were a vote, it would make it very clear how broad  
15 the consensus is about this particular question.

16 Now you are also welcome if we have a  
17 vote, you're welcome to abstain, but I'm not saying  
18 up and down on the three different, or four,  
19 depending on how you want to define the indications.  
20 Yes?

21 DR. HOLTGREWE: Well, I will explain my  
22 vote. I think that when viewed in context with  
23 literature that exists in other fields of medicine,  
24 that what we have looked at here is quite feeble,  
25 even for pressure sores. But of the three disorders,

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1 clearly the evidence is best for pressure sores. If  
2 you look at the other two types of ulcers, it's even  
3 more feeble. But since these are poor patients who  
4 have a terrible problem and it's really a sad  
5 situation, and with little else in the way of  
6 options, and given the information that we do have,  
7 there does appear to be a benefit which I can't  
8 ignore. So that's why I voted yes. But I wouldn't  
9 begin to try to splinter it out into three different  
10 indications. I mean, I just don't think it was  
11 there, so my thought was let's put them all together,  
12 and certainly you want to go with the chronic  
13 problem, so that anybody that gets a dog bite and  
14 somebody gets a sore is not treated with electrical  
15 stimulation right off the bat, and some creative  
16 people might be inclined to do that. But I think  
17 that if you leave it chronic, I don't think we can  
18 split out the three indications; there's just no  
19 literature there to do it.

20 DR. GARBER: Bruce?

21 DR. SIGSBEE: I think if you open that up,  
22 then you also open up the issue of what type of  
23 stimulation is effective, and some have been looked  
24 at. Alternating current was only used in a well  
25 controlled study in venous stasis ulcers and was

00221  
1 shown to be effective. Some of the pulse direct has  
2 been primarily used in the pressure ulcers. The  
3 pulse electromagnetic stimulation is not probably  
4 effective in any of them if you look at it  
5 critically, but it delivers a charge to the tissues,  
6 and we're not sure it makes any difference. So you

7 know, I think if we lump it together, we have a much  
8 more compelling look at this. I can understand and  
9 it is my sense as well, at least we have more studies  
10 on pressure ulcers at this point, but is it really  
11 any different? So I'm not sure that voting on a  
12 sense really reflects accurately the biology of  
13 what's going on here.

14 DR. TUNIS: I think actually this is  
15 helpful, and probably gets us to the same place, if  
16 the folks on the panel just take a turn explaining  
17 their yes vote, because to some degree, it was a  
18 unanimous yes vote, but yet I am not sure everybody  
19 is voting yes for the same reason, and given what we  
20 really need to work with when we go forward in  
21 developing the coverage decision is sort of what went  
22 into the yes vote. It sounds like with this most  
23 recent comment is that what sort of is implicit here  
24 is that some of the panel is saying that we're  
25 willing to agree that essentially there is no reason

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1 why chronic ulcers should heal differently, and  
2 therefore we're willing to kind of aggregate all  
3 these studies together and decide on it en masse.  
4 That may be what some of you are thinking.

5 But you know, if it's sort of to say, it's  
6 somewhat more difficult to understand to say well,  
7 for each individual indication, each individual type  
8 of ulcer, the evidence isn't adequate but when you  
9 take it all together, it becomes adequate, that's the  
10 conundrum we're trying to have you all sort out for  
11 us. So maybe if we could go down and have people  
12 speak.

13 DR. MAVES: Sure, I would be happy to. I  
14 think that's pretty much, Sean, where I'm at this  
15 point. And I mean, my sense is again, I think the  
16 evidence is strongest for pressure, but again, I  
17 think when you actually get on the ground treating  
18 these patients, the difference between pressure,  
19 venous and arterial may really not be very  
20 significant as to how you treat them.

21 The reasons for my yes vote is that I  
22 think even reading the ECRI report where they  
23 indicated there is a very big effect, I think that

24 was a direct quote, was certainly persuasive. And a  
25 part that hasn't been mentioned, I took a look at the  
00223

1 notes that I wrote down from your presentation about  
2 the urinary incontinence decision with biofeedback,  
3 and you gave four reasons. You said there was  
4 positive support for the technology, which there is  
5 here; the patients had few other options short of  
6 surgery, I think that's true here; there's no  
7 suggestion that there's any harm done, and I haven't  
8 heard or read any suggestion that there is any harm;  
9 and there was strong expert testimony. So I think if  
10 you will, looking at HCFA's at least policy regarding  
11 the decision on urinary incontinence and using  
12 biofeedback for that, I think this parallels that  
13 argument, and I felt very comfortable with the  
14 decision I made.

15 DR. GARBER: Angus?

16 DR. MCBRYDE: Well, I'm certainly a lump  
17 in this case, and although I wouldn't use the word  
18 compelling, I think that the evidence that we have  
19 seen, heard and read and reviewed is enough to, for  
20 me, for it to be an efficacious thing, so I would  
21 vote yes. And to sort it out would take for me more  
22 than looking at the physiology a little better about  
23 the three different types of ulcerations and I happen  
24 to think they are close kin, so I would be a lump  
25 in that regard. And I think it much more important

00224  
1 to redefine if there is a definition, but to redefine  
2 that between the primary and the recalcitrant.

3 DR. GARBER: Ken?

4 DR. BRIN: I am just going to mirror what  
5 has been said. I think that the data in the  
6 aggregate is relatively convincing, although I think  
7 the paucity of data is impressive in its own. Given  
8 the degree of, or the amount of nonhealing ulcers  
9 that we have in the population at large, I am  
10 surprised at the lack of the types of literature that  
11 we like to see. But we have mostly aggregated data  
12 and I think we need to deal with the aggregated data.  
13 There hasn't been enough done from subgroups except  
14 for the pressure group, and if we exclude the



15 nonpressure because they are in the aggregate and not  
16 in the pressure, I don't think we can conclude  
17 anything about those other two groups.

18 DR. GARBER: Les.

19 DR. ZENDLE: I have spoken enough.

20 DR. GARBER: Adrian?

21 DR. OLECK: I didn't get to vote.

22 DR. GARBER: Actually, the nonvoting  
23 members can just briefly state reasons for agreeing  
24 or disagreeing with the vote, not that it's required  
25 for the record. You don't have to give your reasons

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1 since you didn't vote, but you're welcome to comment.

2 DR. OLECK: I guess I disagree with the  
3 way that, the lumping everything together. I would  
4 have been more in favor of looking at things  
5 individually, not only according to, less in terms of  
6 wound types than in terms of the different  
7 technologies, and I felt certainly that there was  
8 more evidence for the pressure ulcers, less for the  
9 venous and arterial ulcers.

10 DR. GARBER: Marshall?

11 DR. STANTON: I'm really ambivalent. On  
12 the one hand I see the virtues of lumping it  
13 together. I think the evidence in toto is more  
14 compelling than when you split it, though on the  
15 other hand, as I was going through all the  
16 literature, I did feel that there was probably enough  
17 evidence to make a decision on decubitus ulcers, and  
18 I was less confident on the level of evidence that  
19 was there to make a decision on venous, and I thought  
20 there was not enough evidence on arterial, but I  
21 could see it going either way.

22 DR. GARBER: Thanks. Phyllis?

23 MS. GREENBERGER: I'm comfortable with the  
24 decision. I agree with Dr. Maves in terms of the  
25 four categories that you used for the biofeedback.

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1 And also, I think while if you just looked at the  
2 scientific evidence alone, that there might be  
3 certainly more evidence in one direction than  
4 another, but I think that if you look at all the  
5 clinical evidence and the testimony today, then I

6 don't see that there was that great of difference, so  
7 I agree with the vote.

8 DR. HOLTGREWE: Can I make a comment?

9 DR. GARBER: Yeah, go ahead.

10 DR. HOLTGREWE: I would wish that given  
11 the millions of patients suffering from this  
12 disorder, I would wish that the people involved would  
13 figure out where to set the machine. And that  
14 surely, I just have a conceptual inability to accept  
15 the fact that it doesn't make any difference where  
16 you set the machine, one way or another, it doesn't  
17 matter. I've got to believe that there might be a  
18 difference, and I would hope somebody would do some  
19 studies.

20 DR. GARBER: Thank you for giving your  
21 reasons. Now, you know that there is basically a  
22 check list of things to consider and I think this is  
23 all implicit in your comments, the answer is, so let  
24 me just briefly say what I think is the sense of the  
25 panel, and raise your hand if you disagree.

00227

1 Regarding adequacy of study design, that  
2 you felt the studies were adequate to draw  
3 conclusions, at least in aggregate, and they showed  
4 effectiveness; that they were consistent enough to  
5 satisfy you; and there are obviously public benefits  
6 where there are a huge fraction of the patients that  
7 studies identified were Medicare beneficiaries  
8 generalized beyond the research setting. Any  
9 disagreement with that? Les?

10 DR. ZENDLE: One of the things, I feel it  
11 may have been consistent with the results but I'm not  
12 sure it was with the technologies, and that was a  
13 concern, but not enough.

14 DR. GARBER: Right. Again, we remain  
15 uncertain about whether the technologies are  
16 different in any.

17 Okay. Now we are at the next stage, where  
18 we have to decide about the magnitude of  
19 effectiveness and there are seven categories,  
20 breakthrough technology, more effective, as effective  
21 with advantages, as effective, less effective with  
22 advantages, less effective, not effective.

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Let me remind you at this point that we are dealing with this chronic nonhealing ulcer, so it's compared presumably to whatever else would be used in that context.

1 DR. HOLTGREWE: I move that we consider it more effective.

2 DR. MAVES: I second that.

3 DR. GARBER: There is a motion to accept it as more effective. Discussion? Ken?

4 DR. BRIN: I think a straw vote is again maybe appropriate, as to whether it should be moved up to breakthrough technology. Several of the speakers -- I am not going to promote that, but I'm just going to comment that it might have the potential, if the practitioners can figure out what is the standard of care and figure out the appropriate protocols, can, but at this point it doesn't seem to be.

5 DR. GARBER: Okay.

6 DR. HOLTGREWE: Penicillin was breakthrough. This is not a breakthrough.

7 DR. GARBER: Any other comments or discussion?

8 DR. SIGSBEE: I had trouble wrestling with this in that there are a number of other therapies for chronic wound healing other than saline gauze, and it wasn't compared to some of them, it was never clearly delineated except for moist saline gauze and

00229

1 dressing changes, so I don't know if we can say that this is more effective than other conventional treatments out there, and we have no data.

2 DR. GARBER: Les.

3 DR. ZENDLE: Again, I think the patients with nonchronic wounds were excepted from our definition. Have not responded to conventional therapies, whatever that means, allows me to be comfortable with the more effective. I think the category below that seems to be more patient driven, and I think we've heard enough from the providers that it's not just the patients that are driving this, it's the providers.

14 In terms of breakthrough, I mean  
15 breakthrough implies that it is the standard of care,  
16 in other words, to not use it invites malpractice,  
17 and I certainly don't think it meets that standard.

18 DR. OLECK: I'm just thinking whether  
19 that, the decision saying it's more effective is  
20 consistent with the decision of just saying that it's  
21 for chronic ulcers. If it's more effective than  
22 other technologies, you know, why would it just be  
23 for people that have failed other types of items? It  
24 seems like we're saying it's something that can be  
25 tried in addition to it or after something else has

00230  
1 failed, you're not going to use it, and the  
2 implication is this isn't a first line therapy to be  
3 used. And if you think it's effective, the decision,  
4 the vote was that it was effective, but whether it  
5 has major additional advantages, I don't know whether  
6 that's clear.

7 DR. GARBER: Yes, Angus.

8 DR. MCBRYDE: Two things, which are very  
9 self evident perhaps, make me think that's the right  
10 category two, and belongs there. One is that  
11 although it's referred to in all our literature,  
12 there is a huge body of basic science that shows that  
13 electrical stimulation has a heck of a cellular and  
14 basic effect. And that coupled with the fact that as  
15 we know, the modalities applied in every way, so  
16 whether you feel that the modalities are short on the  
17 short end on some of the applications of it, or on  
18 the long end, as time goes by, whatever we feel is  
19 efficacious now will be more so in the future,  
20 because the basic science is there. Plus, we don't  
21 know the exact center of the spectrum as far as  
22 application is, so that makes me feel better about  
23 it, if anything, moving up in the scale as time goes  
24 by, if that makes sense.

25 DR. GARBER: Any other comments? I will

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1 call for the vote. The motion is to place it in the  
2 second category, more effective. All in favor?

3 Unanimous. Okay, thank you.

4 DR. TUNIS: I just need to verify this, we

5 probably did this, but the vote before the break,  
6 there was a -- it is actually fairly simple to  
7 resolve, but was the vote on actually changing the  
8 question to lump things, or did you actually vote on  
9 that amended question?

10 DR. GARBER: We voted on the question.

11 DR. TUNIS: Is that your recollection as  
12 well? Okay. So we are good.

13 DR. GARBER: The floor is yours.

14 DR. TUNIS: So assuming there is no more  
15 comments or reflections on the part of the panel, you  
16 have all had your adequate say, any other thoughts?  
17 Good.

18 Well, then the next step is really to  
19 thank all our presenters today, as well as the panel  
20 for their good work. We now, by our formal process,  
21 there will be, this will be summarized and taken  
22 forward by Dr. Garber to the next Executive Committee  
23 meeting, at which we can discuss this issue for  
24 discussion of the ratification of the recommendation  
25 of the panel, and then from the time that we receive

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1 the conclusion about the Executive Committee's  
2 recommendation, we would then have 60 days to issue a  
3 HCFA coverage decision. So those are the next steps  
4 and again, thanks for all of your efforts.

5 DR. HOLTGREWE: Connie, can we leave our  
6 materials here?

7 MS. CONRAD: The room will be secured, you  
8 may leave your materials here. I need a motion to  
9 adjourn the meeting.

10 DR. SIGSBEE: So move.

11 DR. MAVES: Second.

12 MS. CONRAD: Thank you.

13 (The meeting adjourned at 3:25 p.m.)  
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